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(54) Title: METHODS FOR IDENTIFYING THERAPEUTIC TARGETS INVOLVED IN GLUCOSE AND LIPID METABOLISM

(57) Abstract: The identification and evaluation of mRNA and protein targets associated with RNA binding proteins or mRNP complexes is described. In particular, the invention provides methods for identifying RNA binding proteins associated with physiological pathways that participate in glucose and lipid metabolism and mRNAs that exhibit coordinated gene regulation across those pathways. Candidate targets are provided that are useful for the diagnosis or treatment of diseases related to diseases, such as disease related to aberrant glucose and lipid metabolism, such as, for example, obesity, diabetes, and hypoglycemia.

Methods for Identifying Therapeutic Targets Involved in Glucose and Lipid Metabolism

RELATED APPLICATIONS

This application claims priority to and the benefit of U.S.S.N. 60/461,016, filed April 7, 2003, the contents of which are incorporated by reference herein.

FIELD OF THE INVENTION

5 The invention provides methods and compositions for identifying and characterizing functionally related gene products associated with isolated mRNP complexes. The invention also provides methods and compositions for identifying and characterizing metabolic pathways, such as glucose or lipid metabolic pathways, and therapeutic targets and therapeutics for treating diseases associated with metabolic pathways.

10 *BACKGROUND OF THE INVENTION*

Glucose and lipid metabolism are regulated by the coordinated expression of a number of proteins that participate in insulin production, secretion, and action. Beta cells of the pancreas sense increased plasma glucose, lipids, and other nutrients, and activate a cascade of intracellular reactions leading to the controlled release of insulin from storage granules. Insulin, in turn, controls plasma glucose and lipid levels by stimulating glucose uptake into insulin-sensitive tissues (*e.g.e.g.*, skeletal muscle and adipose), lipid metabolism, and inhibiting hepatic glucose production.

Diabetes is a disease characterized by an impairment of insulin action. Type 1 diabetes results from an inability of pancreatic beta cells to produce insulin, forcing patients to take daily insulin injections to control their blood glucose. Type 2 diabetes is a metabolic disorder in which a patient becomes resistant to insulin's actions, leading to hyperglycemia, hyperlipidemia, and hyperinsulinemia. In many cases, Type 2 diabetes is associated with obesity and a sedentary lifestyle. Efforts have been made to establish pancreatic beta cell lines from adult and embryonic stem cells and to engineer pancreatic beta cell-like cell lines in order to study the

metabolic pathways that are activated during development, growth, and maintenance of pancreatic beta cells.

Although some of the cellular pathways involved in glucose and lipid metabolism are understood, a number of regulatory aspects of those pathways have not been fully characterized.

5 The identification of RNAs that are co-regulated with insulin gene expression would provide information about the regulation of genes involved in controlling insulin production and secretion by beta cells of the pancreas. Identification of co-expressed RNAs would also help identify previously unknown components of the insulin signaling pathway and other glucose and/or lipid metabolic pathways in adipocytes, as well as other cells that participate in glucose or
10 lipid metabolism. Identification of the components of glucose and lipid metabolic pathways provides new therapeutic targets for diabetes, obesity, and other diseases characterized by altered glucose or lipid metabolism. A need therefor exists for a sensitive, focused, and efficient method for identifying such functionally related genes, therapeutic targets, and therapeutics.

SUMMARY OF THE INVENTION

15 The invention exploits the ability of RNA binding proteins to bind and coordinate the expression of functionally and structurally related RNAs. The RNAs bound to a particular RNA binding protein define a cluster of functionally related gene products and may also possess common primary and/or secondary structures that mediate binding to the RNA binding protein. RNA binding proteins and RNAs identified by methods of the invention are useful for
20 elucidating physiological or regulatory pathways, such as glucose or lipid metabolic pathways, including insulin action, insulin resistance, obesity, and diabetes. The RNAs, the genes encoding those RNAs, and proteins identified by the methods of the invention are putative therapeutic targets due to their ability to regulate other genes that participate in, or otherwise modulate, aberrant physiological, metabolic or regulatory pathways in a disease state.

25 The invention provides a ribonomic profile, and methods for identifying and characterizing a ribonomic profile, including the expression of RNAs, RNA binding proteins, and mRNP complex-associated proteins associated with a particular mRNP complex or set of mRNP complexes. For example, genes participating in a glucose or a lipid metabolic pathway are identified by characterizing the mRNAs associated with a particular mRNP complex known,
30 or determined, to be a participant in the pathway. According to the invention, mRNAs or proteins are classified into biologically relevant subsets on the basis of structural and/or

functional relationships (*e.g.e.g.*, that participate in the same insulin production or secretion pathway, or that facilitate gene expression during growth and development in normal or diseased pancreatic beta cells). In contrast to the static genomics and proteomics approaches to gene characterization and drug discovery, this “ribonomics” approach provides a dynamic snapshot of the flow of genetic information at a given time in the life of a cell or tissue, for example, in a normal or diseased state or in response to an environmental influence, such as glucose or a drug.

In an aspect, the invention provides methods for identifying RNA binding protein, mRNA and protein components of an mRNP complex in cells associated with a physiological process or pathway, by immunoprecipitating an mRNP complex, identifying and comparing the components of the mRNP complex, such as, for example, RNA binding proteins, mRNAs, and other proteins, and validating the biological role of those proteins, or the genes that encode those proteins, in the physiological process or pathway. In an embodiment, the method further includes preparing an RNA binding protein profile, isolating the RNA binding protein, and/or producing antibodies to the RNA binding protein.

In one aspect, the invention provides methods of identifying a therapeutic target related to the treatment of a disease, such as aberrant glucose or lipid metabolism. The protein or RNA levels of at least one component of an isolated mRNA ribonucleoprotein (mRNP) complex in a cell sample is measured and compared to the levels of the protein or RNA levels of the component in a second cell sample. The two cell samples may differ in that one is normal and one is diseased or may differ regarding their state of differentiation. The cell samples may also differ in that one sample is treated with an agent and one sample is not. For example, the cell samples may contain mostly mature adipocytes, preadipocytes, pancreatic beta cells, hepatocytes, skeletal muscle cells, or cardiac muscle cells, or any cell that participates in glucose or insulin metabolism, for example. If the levels of the component in the first sample are different from the levels of the component in the second sample, the component, a nucleic acid that encodes the component (if the component is a protein), or a protein encoded by the component (if the component is a nucleic acid) is a potential therapeutic target for the treatment of a disease related to altered glucose or lipid metabolism. In an embodiment, the component is an RNA binding protein, an RNA, or an mRNP-associated protein.

In an embodiment, the first cell sample has the phenotype of a mature adipocyte and the second cell sample has the phenotype of a preadipocyte. A difference in the expression of a

component of the mRNP complex between the two cell types is indicative that the component participates in a pathway involved in the differentiation from preadipocyte to adipocyte.

In another embodiment, the first cell sample has a disease phenotype related to glucose or lipid metabolism, such as obesity, diabetes, hypoglycemia, glucotoxicity, lipidotoxicity, insulin-
5 resistance, hyperlipidemia, and lipodystrophy, and the second cell sample has a normal phenotype.

In another embodiment, the method has an additional step of treating the sample with an agent prior to measuring the protein or RNA levels of the mRNP complex component, wherein the agent alters the levels of at least one component of a glucose metabolic or a lipid metabolic
10 pathway. In an embodiment, the agent is insulin, glucose, insulin-like growth factor-1 (IGF-1), a β -adrenergic agonist, glucagon-like peptide-1 (GLP-1), fatty acid, a peroxisome proliferator activated receptor (PPAR) ligand, or insulin-like growth factor 2 (IGF-2), RNAi against an RNA binding protein, overexpression of an RNA binding protein, or an enhancer of an RNA binding protein for example. In another embodiment, the agent is a test therapeutic, such as, for
15 example, a nucleic acid, a hormone, an antibody, an antibody fragment, an antigen, a cytokine, a growth factor, a pharmacological agent (*e.g.e.g.*, chemotherapeutic, carcinogenic, or other cell), a chemical composition, a protein, a peptide, and/or a small molecule (*e.g.*, a putative drug).

In an aspect, the invention comprises methods for identifying RNA binding protein, mRNA and protein components of an mRNP complex in cells associated with physiological
20 pathways or processes, for example glucose or lipid metabolism. The method includes the steps of identifying RNA binding proteins enriched in cells, such as, for example, adipocytes or preadipocytes (for example in lean or obese individuals), treating the cells with an agent, such as, for example, insulin or a beta 3 agonist, and identifying the components of the mRNP complex (*e.g.*, functional cluster). In an embodiment, the methods of the invention further include the
25 step of identifying a suitable RNA binding protein for analysis, *e.g.*, an RNA binding protein that participates in the regulation of the physiological pathway or process. In a further embodiment, the method further includes the step of validating the function of the component within the pathway.

In another embodiment, the methods of the invention have a further step of isolating the
30 component, a nucleic acid encoding the component, or a protein encoded by the component. For example, the methods of the invention can identify and isolate an mRNA encoding the RNA binding protein and/or an mRNP complex-associated protein, a gene encoding the RNA binding

protein and/or an mRNP complex-associated protein, an mRNP complex comprising the RNA binding protein and/or an mRNP complex-associated protein, an mRNA associated with the mRNP complex, and a gene encoding the mRNA associated with the mRNP complex. In addition, the invention contemplates identifying other associated RNAs that bind to one or more components of the mRNP complex. These RNAs include, but are not limited to, microRNA (miRNA), non-coding RNA (ncRNA or snmRNA), ribosomal RNA (rRNA), small interfering RNA (siRNA), small nuclear RNA (snRNA), small nuclear RNA (snoRNA), small temporal RNA (stRNA), and transfer RNA (tRNA).

In an embodiment, the component is an RNA binding protein, such as Polypyrimidine Tract Binding Protein (PTB, also known as RNA binding protein 1 (RBP1)). In another embodiment, the RNA binding protein is selected from the group consisting of the RNA binding proteins identified in Figures 10-22. These RNAs were subjected to analysis on a microarray containing RNA binding protein genes. These genes and their encoded proteins represent candidate therapeutic targets as well as candidates for RASTM analysis for elucidation of cellular pathways involved in glucose and lipid metabolism, insulin action, insulin resistance, diabetes and obesity, for example. In an embodiment, the RNA binding protein has a tag (*e.g. e.g.*, HIS (GST) to facilitate affinity purification.

In an embodiment, the component is an mRNA that is associated with a particular RNA binding protein. The mRNA are identified singly or mRNAs are identified *en masse*, *e.g.*, using arrays containing a number of probes. In an embodiment, the mRNA encodes a kinase, a transporter, a phosphatase, a channel protein, a protease, a receptor, a transcription factor, or a transferase. For example, the protein may be 3-phosphoinositide dependent protein kinase-1; nuclear ubiquitous casein kinase 2; neural receptor protein-tyrosine kinase; MAP-kinase activating death domain; AMP-activated protein kinase beta-2 regulatory subunit; calcium/calmodulin-dependent protein kinase IV; Protein kinase C beta; adenylate kinase 3; mitogen activated protein kinase; kinase 5; 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 2; phosphatidylinositol 4-kinase; Glucokinase; glycogen synthase kinase 3 beta; phosphorylase kinase (gamma 2, testis); protein tyrosine phosphatase (non-receptor type 1); protein tyrosine phosphatase (non-receptor type 5); inositol polyphosphate-5-phosphatase D; Protein tyrosine phosphatase (receptor-type, zeta polypeptide); dual specificity phosphatase 6; protein tyrosine phosphatase (non-receptor type 12); glucose-6-phosphatase (catalytic); 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 2; proton gated cation channel DRASIC; Sodium channel (nonvoltage-gated 1, alpha (epithelial)); calcium channel (voltage-dependent,

alpha2/delta subunit 1); Potassium inwardly-rectifying (channel, subfamily J, member 6);
 potassium channel regulator 1; calcium channel (voltage-dependent, T type, alpha 1G subunit)
 cyclic nucleotide-gated cation channel; amiloride-sensitive cation channel 1; potassium
 inwardly-rectifying channel J14; potassium large conductance calcium-activated channel
 5 (subfamily M, alpha member 1); potassium voltage gated channel (Shab-related subfamily,
 member 2); potassium channel subunit (Slack); potassium intermediate/small conductance
 calcium-activated channel (subfamily N, member 1); Sodium channel (voltage-gated, type V,
 alpha polypeptide); amiloride-sensitive cation channel 2 (neuronal); potassium channel
 (subfamily K, member 6 (TWIK-2)); cation-chloride cotransporter 6; solute carrier family 21
 10 (organic anion transporter, member 12); amino acid transporter system A2; peptide/histidine
 transporter; choline transporter; solute carrier family 31 (copper transporters, member 1); solute
 carrier family 13 (sodium-dependent dicarboxylate transporter); solute carrier family 2
 (facilitated glucose transporter, member 13); solute carrier family 12 (potassium-chloride
 transporter, member 5); Solute carrier family 6 (neurotransmitter transporter, serotonin, memb
 15 4); Solute carrier family 2 A2 (glucose transporter, type 2); carboxypeptidase D; ubiquitin
 specific protease 2; mast cell protease 1; proprotein convertase subtilisin / kexin, type 7; lamin
 receptor 1 (67kD, ribosomal protein SA); protein tyrosine phosphatase (non-receptor type 1);
 calcium-sensing receptor; neural receptor protein-tyrosine kinase; glutamate receptor
 (metabotropic 4); nuclear receptor subfamily 4 (group A, member 2); Neuropeptide Y5 recept
 20 protein tyrosine phosphatase (non-receptor type 5); insulin-like growth factor 1 receptor; Prote
 tyrosine phosphatase (receptor-type, zeta polypeptide); nuclear receptor subfamily 4 (group A,
 member 3); glutamate receptor (metabotropic 1); Tumor necrosis factor receptor superfamily
 (member 1a); insulin receptor; gamma-aminobutyric acid receptor associated protein; protein
 tyrosine phosphatase; non-receptor type 12; cholinergic receptor (nicotinic, beta polypeptide 1
 25 olfactory receptor (U131); Gamma-aminobutyric acid receptor beta 2; glial cell line derived
 neurotrophic factor family receptor alpha 1; Glycine receptor beta; glutamate receptor interact
 protein 2; adenylate cyclase activating polypeptide 1 receptor 1; asialoglycoprotein receptor 2;
 adenosine A3 receptor; Fibroblast growth factor receptor 1; nuclear receptor binding factor 2;
 purinergic receptor P2Y (G-protein coupled 1); nuclear receptor subfamily 1 (group H, membe
 30 4); peroxisome proliferator activator receptor(gamma); 5 hydroxytryptamine (serotonin) recep
 4; retinoid X receptor gamma; insulin receptor-related receptor; putative N-acetyltransferase
 Camello 4; lecithin-retinol acyltransferase; Phenylethanolamine N-methyltransferase;
 fucosyltransferase 2; Sialyltransferase 8 (GT3 alpha 2,8-sialyltransferase) C; UDP-

glucuronosyltransferase; alpha 1,3-fucosyltransferase Fuc-T (similar to mouse Fut4); diacylglycerol O-acyltransferase 1; signal transducer and activator of transcription 3; ISL1 transcription factor (LIM/homeodomain); and oligodendrocyte transcription factor 1. In another embodiment, the protein is encoded by a gene selected from the group consisting of CNCG, CACNA2D1, KCNC3, and KCNB2.

In another aspect, the invention provides a method for identifying a therapeutic target for the treatment of a disease that involves a physiological or regulatory pathway, such as aberrant glucose metabolism or lipid metabolism, by comparing RNA or protein levels of at least one component of an isolated mRNP complex in a sample from an individual with a disease associated with altered glucose metabolism or lipid metabolism to RNA or protein levels of the component in a healthy sample. If the levels of the component in the diseased sample are different from the levels of the component in the healthy sample, the component, a nucleic acid that encodes the component, or a protein encoded by the component is a potential therapeutic target for the treatment of the disease.

In another aspect, the invention provides a method for identifying a gene or gene product involved in a physiological or regulatory pathway in a cell, such as a glucose or lipid metabolic pathway. For example, an mRNP complex containing at least one component that participates in a glucose metabolic or lipid metabolic pathway is isolated and at least one additional component of the isolated mRNP complex is identified. The additional component is also likely involved in a glucose or lipid metabolic pathway. In an embodiment, the method includes the step of confirming the activity of the additional component by inhibiting the expression of the additional component in a cell or organism and determining the effect of the inhibition on glucose metabolism or lipid metabolism. Inhibition can be achieved by any number of means, including for example, inhibiting gene expression of the additional component using an RNAi, an antisense RNA, a ribozyme, a PNA, or an antibody.

In another aspect, the invention provides a method for identifying an agent that alters a physiological or regulatory pathway in a cell, such as a glucose metabolism or lipid metabolism. A cell sample is treated with an agent and an mRNP complex having at least one component that participates in a metabolic pathway, for example, a glucose metabolic or lipid metabolic pathway, is isolated from the sample, and the RNA or protein levels of at least one component of the isolated mRNP complex are measured and compared to the RNA or protein levels of the component isolated from an untreated control sample. Differential expression of the component

in the agent-treated sample compared to the untreated control sample is indicative that the agent regulates or participates in glucose metabolism or lipid metabolism. In an embodiment, the agent interacts with or regulates a component of a pathway, such as an insulin production pathway, a lipogenesis pathway, an insulin action pathway, a lipid metabolism pathway, or a glucose metabolism pathway, or any pathway that participates in an aspect of glucose and lipid metabolism. In yet another embodiment, the agent inhibits a pathway. In another embodiment the agent enhances a pathway. In an embodiment, the agent is insulin, a beta-adrenergic agonist, insulin-like growth factor-1 (IGF-1), glucagon-like peptide-1 (GLP-1), fatty acid, peroxisome proliferator activated receptor (PPAR) ligands (*e.g.*, thiazolidinediones, fibrates, halogenated fatty acids, and tyrosine derivatives), insulin-like growth factor-2 (IGF-2), an RNAi against an RNA binding protein, an enhancer of RNA binding protein expression, and/or glucose.

In a particular aspect, the invention provides a method for identifying a gene product that regulates glucose metabolism in a cell. The expression in an isolated mRNP complex of at least one gene product of a pancreatic beta cell sample is measured. The gene product may be an RNA binding protein, an mRNA associated with the RNA binding protein, or an mRNP complex-associated protein. The cell sample, such as a pancreatic beta-cell sample, is then treated with an agent, such as, for example, insulin, glucose, insulin-like growth factor-1 (IGF-1), a β -adrenergic agonist, glucose, glucagon-like peptide-1 (GLP-1), fatty acid, a peroxisome proliferator activated receptor (PPAR) ligand, or insulin-like growth factor 2 (IGF-2). The expression of the gene product is then measured after treatment. A difference in the expression of the gene product after treatment compared to the expression of the gene product before treatment is indicative that the gene product participates in the regulation of glucose metabolism.

In another aspect, the invention provides a method for identifying an agent that regulates insulin production and/or its regulated secretion in a pancreatic beta cell. A pancreatic beta cell sample is treated with a nucleic acid capable of binding to at least one RNA binding protein that is capable of binding to a 3' untranslated region or a 5' untranslated region of a preproinsulin mRNA. The nucleic acid is then separated from the RNA binding protein and the RNA binding protein is identified. In an embodiment, the RNA binding protein binds to a nucleic acid having a sequence 5'-gaauaaaaccuuugaaagagcacuac-3', 5'-cccaccacuaccuguccacccucugcaaug-3', or 5'-agccctaagtgaccagctacgtcggaaccatcagcaagcaggtcattgtccaac-3'.

In another embodiment, the invention provides a method for identifying a component of an mRNP complex by transfecting a cell sample with a nucleic acid that inhibits the expression

of an RNA binding protein associated with the mRNP complex. Total RNA from the cell sample and from a control sample is then isolated and measured. RNAs that have altered expression in the nucleic acid-transfected sample compared to the control sample are considered members of the mRNP complex that share functional and/or structural characteristics (*e.g.e.g.*, that participate in the same metabolic pathway).

In another aspect, the invention provides an isolated mRNP complex, for example, an mRNP complex, containing polypyrimidine tract binding (PTB) and at least one mRNA associated with the PTB protein.

In another aspect, the invention provides methods for identifying a protein that regulates insulin production and/or its regulated secretion by measuring the expression of an RNA binding protein, an mRNA associated with the RNA binding protein, and/or an mRNP complex-associated protein in a pancreatic beta cell sample, treating the pancreatic beta cell sample with an agent, such as, insulin, a beta-adrenergic agonist, insulin-like growth factor-1 (IGF-1), glucagon-like peptide 1 (GLP-1), fatty acid, peroxisome proliferator activated receptor (PPAR) ligands (*e.g.*, thiazolidinediones, fibrates, halogenated fatty acids, and tyrosine derivatives), insulin-like growth factor-2 (IGF-2), RNAi against an RNA binding protein involved in insulin production or secretion, an enhancer of an RNA binding protein expression and/or glucose, and measuring expression of the levels of RNA binding protein, mRNA, and/or an mRNP complex associated protein after treatment. The difference in the expression of the RNA binding protein, an mRNA associated with the RNA binding protein, and/or an mRNP complex-associated protein after treatment compared to expression before treatment is indicative that the RNA binding protein, mRNA, associated with the RNA binding protein, and/or an mRNP complex-associated protein regulates insulin production.

In another aspect, the invention provides methods of identifying gene products co-regulated with an mRNA that participates in the glucose or lipid metabolic pathway, such as, for example, preproinsulin mRNA, by isolating an RNA binding protein or mRNP complex-associated protein that binds to the mRNA known to participate in glucose or lipid metabolism and identifying at least one additional component of the mRNP complex (*e.g.*, mRNA, RNA binding protein, and/or mRNP complex-associated protein).

In another aspect, the invention provides methods for assessing the efficacy of an agent as a therapeutic for treating an individual having a disease associated with altered glucose and/lipid metabolism. The methods comprise the steps of contacting a sample from an individual

having a disease with an agent, and comparing the level of expression of an RNA binding protein, an mRNA associated with the RNA binding protein, or an mRNP complex-associated protein in the agent-treated sample to the level of expression of the RNA binding protein, the mRNA associated with the RNA binding protein, or the mRNP complex-associated protein in :
5 control sample, wherein a difference in expression is indicative that the agent is a candidate therapeutic capable of treating the disease. The methods of the invention are also used to monitor the efficacy or toxicity of an agent.

In another aspect, the invention provides a method to identify genes affected by the activity of a specific RNA binding protein. RNAi-mediated gene silencing is used to inhibit the
10 expression of a specific RNA binding protein. RNA samples are isolated from control RNAi treated cells or tissues and RNA binding protein-specific RNAi treated cells or tissues and genes that are differentially expressed are identified.

The foregoing and other objects, features and advantages of the present invention will be made more apparent from the following drawings and detailed description of preferred
15 embodiments of the invention.

BRIEF DESCRIPTION OF THE DRAWINGS

The objects and features of the invention may be better understood by reference to the drawings described below in which,

Figure 1 is a schematic overview outlining an embodiment of the RIBOTRAPTM assay
20 for the isolation of an RNA binding protein (RBP-X) binding to a biotinylated mRNA of interest using a streptavidin-agarose support.

Figure 2 is a schematic overview of the RNA binding protein identification using one type of RIBOTRAPTM assay and subsequent RASTM assay for identification of mRNA substrates for the RNA binding protein identified by RIBOTRAPTM.

25 Figure 3 shows the general scheme of Ribonomic Analysis System, RASTM. RASTM involves the isolation of mRNP complexes based upon specific RNA binding proteins and the identification of RNAs dissociated with the mRNP complex. RASTM can be performed in at least three ways; A) *In vivo* RASTM using antibodies against the native endogenous RNA binding protein, B) *In vivo* RASTM using epitope-tagged RNA binding protein and an antibody

against the epitope, C) *In vitro* RASTM using purified recombinant RNA binding protein and cell extracts or purified RNA.

Figure 4 is a schematic of using RIBOTRAPTM and RASTM for polypyrimidine tract binding protein (PTB, or RBP-1). A ribonucleic cluster is isolated from cell extracts using antibodies specific for RBP-1. RNA extracted from this cluster is compared to total RNA by global microarray analysis.

Figure 5 is a schematic overview of an embodiment of a target discovery process using RNA binding proteins and mRNP complexes.

Figure 6 is a schematic overview of an exemplary data flow for analyzing and interpreting microarray results from comparative RNA binding protein expression and/or mRNP complexes for identifying tissue or disease-specific RNA binding proteins, mRNAs, and genes.

Figure 7 is a Western blot illustrating the *in vitro* RIBOTRAPTM, verifying that PTB from INS-1 cell lysates specifically binds the oligonucleotides encoding a portion of the 3'UTR of preproinsulin and not oligonucleotides encoding a control oligonucleotide. In addition, glucose stimulates an acute and transient increase in PTB binding. Lanes 1 and 2: total cell lysate; Lanes 3 and 4: control oligonucleotides; Lanes 5 and 6: 5' UTR oligonucleotides; Lanes 7 and 8: 3'UTR oligonucleotides.

Figure 8 illustrates a proposed model of glucose-regulated RNA binding protein binding to preproinsulin mRNA and regulation of glucose-induced preproinsulin translation by RNA binding proteins. Sp, signal peptides; B, C, A, coding regions for various peptide chains of processed insulin.

Figure 9 is a schematic overview of target discovery in primary adipocytes.

Figure 10 is a list of RNA binding protein genes whose expression is differentially regulated (2-fold or more) during differentiation of human pre-adipocytes to adipocytes. RNA was isolated from lean patients pre-adipocytes and RNA from lean patients differentiated adipocytes.

Figure 11 is a list of RNA binding protein genes that are up-regulated 2-fold or more during differentiation of adipocytes from obese patients.

Figure 12 is a list of RNA binding proteins that are differentially expressed (2-fold or more) in human adipocytes treated with BRL-37433. RNA was isolated from human adipocytes

prepared from lean (non-obese) patients that were either left untreated or with the β -3 adrenergic agonist, BRL-37344 (1 μ M).

Figure 13 is a list of RNA binding proteins that are differentially expressed (2-fold or more) in human adipocytes treated with insulin. RNA was isolated from human adipocytes prepared from lean (non-obese) patients that were either left untreated or with insulin (100 nM).

Figure 14 is a list of RNA binding proteins that are differentially regulated by glucose in INS-1 cells.

Figure 15 is a list of RNA binding protein genes differentially expressed in HepG2 cells treated with bezafibrate.

Figure 16 is a list of RNA binding protein genes differentially expressed in HepG2 cells treated with Wyeth 14643.

Figure 17 is a list of RNA binding protein genes differentially expressed in HepG2 cells treated with troglitazone.

Figure 18 is a list of RNA binding protein genes differentially expressed in HepG2 cells treated with MCC-555.

Figure 19 is a list of RNA binding protein genes differentially expressed in HepG2 cells treated with ciglitazone.

Figure 20 is a list of RNA binding protein genes differentially expressed in HepG2 cells treated with 2-bromohexadecanoic acid (2-BHDA).

Figure 21 is a list of RNA binding protein genes differentially expressed in HepG2 cells treated with prostaglandin J2 (PJ2).

Figure 22 is a list of RNA binding protein genes differentially expressed in HepG2 cells treated with perfluorooctanoic acid (PFOA).

Figure 23 is a list of genes identified in an *in vitro* RASTM analysis of GST-PTB. These genes and their encoded proteins represent candidate therapeutic targets of cellular pathways involved in glucose and lipid metabolism, insulin action, insulin resistance, diabetes and obesity.

Figure 24 shows examples of target validation using RNAi mediated gene silencing followed by an assay to determine glucose-stimulated insulin secretion. Figure 24A shows effect of RNAi mediated gene silencing of PTB on insulin secretion. Figure 24B shows effect of RNA

mediated gene silencing of three ion channels contained within the PTB ribonomic cluster.

Figure 24C shows the effect of RNAi mediated gene silencing of IonCh4 or CNCG on insulin secretion.

Figure 25 is a schematic for the regulatory mechanisms of insulin secretion in pancreatic beta cells. Proteins that are shown in bold print are present on the PTB cluster.

Figure 26A shows an immunoblot probed with a PTB monoclonal antibody showing PT binding to a preproinsulin 3'UTR oligonucleotide after cells were grown in various amounts of glucose. Figure 26B is a bar graph depicting the data from Figure 26A.

Figure 27 is a refined list of candidate therapeutic targets obtained from the PTB ribonomic cluster and is organized into druggable target classes.

Figure 28 shows the effect of PTB inhibition by RNAi on the expression of PTB, preproinsulin as well as nine additional genes found within the PTB-cluster: CACNA1s, CACNA2D1, Casr, C1c3, KCNJ6, and Loc245960. As indicated in Figure 28A, there was an 80% reduction in PTB mRNA expression, confirming the action of the PTB specific RNAi. Expression of some of the other genes was also downregulated to varying degrees. Figure 28B shows genes whose expression was up-regulated as a result of PTB knockdown, which includes preproinsulin mRNA, which is up-regulated 3-fold.

DETAILED DESCRIPTION

The invention provides methods for mining and characterizing the cellular ribonome in cells that participate in regulatory pathways, such as, for example, insulin action, insulin production and secretion, glucose metabolism, and lipid metabolism. The resulting ribonomic profile provides a subset of genes, and the mRNAs and proteins they encode, as potential therapeutic targets for altering or regulating those pathways.

Methods of the invention comprise identifying and measuring mRNP complex components. Differentially expressed mRNP complex components are potential therapeutic targets, and are useful for assessing the efficacy or toxicity of potential therapeutics. The invention also provides methods for identifying and characterizing structurally and/or functionally related gene products, and for elucidating features of biological pathways or other cellular functions. The identified mRNP complex components are also useful for diagnosing, monitoring, and assessing the metabolic or disease state of a cell or organism.

Generally, mRNP complex components include, but are not limited to, at least one RNA binding protein, and at least one associated or bound mRNA. The mRNP complex may also include at least one associated or bound protein (*i.e.*, an mRNP complex-associated protein) or other associated or bound molecules (*e.g.*, carbohydrates, lipids, vitamins, *etc.*). A component
5 associates with an mRNP complex if it binds or otherwise attaches to the mRNP complex with Kd of about 10^{-5} to about 10^{-12} . In an embodiment, the component associates with the complex with a Kd of about 10^{-7} to about 10^{-9} . In another embodiment, the component associates with the complex with a Kd of about 10^{-8} to about 10^{-9} .

By isolating an mRNP complex from a cell and, preferably, identifying the components
10 of the mRNP complex and the gene precursors and gene products of those components, a ribonomic profile is generated. The associated or bound RNAs are categorized into subsets based on their association with a particular RNA binding protein, mRNP complex-associated protein, mRNA, or other common structural or functional feature. Ribonomic profiles differ from cell sample to cell sample, depending on a variety of factors including, but not limited to,
15 the species or tissue type of the cell, the developmental stage of the cell, the differentiation state of the cell (*e.g.*, malignant) the pathogenicity of the cell (*e.g.*, if the cell is infected, is expressing a deleterious gene, is lacking a particular gene, is not expressing or is underexpressing a particular gene, or is overexpressing a particular gene), the various conditions or agents affecting the cell (*e.g.*, treatment with a therapeutic, environmental, apoptotic or stress state, and the
20 specific ligands used to isolate the mRNP complexes, as well as other factors known to practitioners in the art. The profile therefore provides a footprint of the gene expression of the cell samples that can be used to identify therapeutic targets and to elucidate components of cellular pathways in normal or disease cells.

Identification and Isolation of mRNP Complexes and RNA Binding Proteins

25 RNA binding proteins involved in a particular pattern, pathway, or disease state, are identified by a variety of methods in the art. For example, the expression of RNA binding proteins that are differentially expressed between normal and disease samples or normal and agent-treated samples can be assessed using methods such as Northern blot, Quantitative Real Time Polymerase Chain Reaction (QRT-PCR), Western blot, microassay analysis,
30 Serial Analysis of Gene Expression (SAGE), cloning and sequencing, or other methods known to the skilled artisan.

Alternatively, differentially expressed RNA binding proteins can be efficiently identified using either a microarray such as a RIBOCHIP™. A RIBOCHIP™ (MWG Biotech, High Point, NC) is a microarray that is used to assay the expression level for a large number of RNA binding proteins. The RIBOCHIP™ contains 50-mer oligonucleotides
5 representing genes, the protein products of which are reported to have RNA binding properties or to contain RNA binding motifs. These genes include those identified in Figures 10-22, and described in Examples 1-5. Also included on the array are control features (a total of 17) that provide information on specificity, labeling and hybridization efficiency, sensitivity and normalization between experiments.

10 In an embodiment, cell samples containing mRNAs encoding RNA binding proteins are used to probe a microarray containing nucleic acid sequences encoding at least a portion of a number of RNA binding proteins, in order to detect and/or measure the expression of RNA binding proteins in the sample. Sample mRNAs are prepared from cell lines or tissues from control, agent-treated, normal, or diseased states, for example. The agent may be any
15 agent that alters gene expression, for example, glucose, insulin, a beta-adrenergic agonist (*e.g.*, BRL-37433), insulin-like growth factor-1 (IGF-1), glucagon-like peptide-1 (GLP-1), fatty acid, peroxisome proliferator activated receptor (PPAR) ligands (*e.g.*, thiazolidinediones, fibrates, halogenated fatty acids, and tyrosine derivatives), insulin-like growth factor-2 (IGF-2). The agent may also be an RNAi that inhibits an RNA binding
20 protein, an enhancer of RNA binding protein expression, a nucleic acid, a hormone, an antibody, an antibody fragment, an antigen, a cytokine, a growth factor, a pharmacological agent (*e.g.*, chemotherapeutic, carcinogenic), a chemical composition, a protein, a peptide, and/or a small molecule. The mRNA samples are amplified if necessary, and processed for microarray hybridization.

25 Microarray analysis enables RNA binding protein genes with unique or differential expression profiles to be quickly identified and clustered into functional or structural categories from among the thousand genes profiled in a single experiment. Several specific examples of microarray analysis and lists of relevant RNA binding protein genes and encoded proteins that are differentially expressed are provided in Examples 3-5. These
30 differentially expressed RNA binding proteins genes are involved in, for example, obesity, adipocyte differentiation, insulin action, insulin production and secretion, diabetes, mechanisms of action of PPAR ligands, insulin resistance, glucose metabolism, lipid

metabolism, hypoglycemia, glucotoxicity, lipid toxicity, insulin resistance, hyperlipidemia, and lipodystrophy.

Pancreatic beta cell lines or freshly prepared islets are physiologically relevant *ex vivo* model systems for examining glucose-responsiveness and endocrine pancreas functions. To identify RNA binding proteins that undergo changes in expression, cells are incubated under conditions of low (*e.g.*, 3 mM) or high (*e.g.*, 15 mM) glucose for various periods of time. Total mRNA is prepared according to standard methods. In some cases where samples are limiting, it may be necessary to amplify the mRNA according to standard RT-PCR methods or kits such as the RIBOAMP™ kit (Arcturus, Mountain View, CA). Differentially expressed RNA binding protein genes identified by microarray analysis represent RNA binding proteins whose expression is regulated by glucose.

In another embodiment, mRNA and protein levels of RNA binding proteins are determined in cell lines such as the alpha cell line, α -TC1.6, the rat pancreatic beta cell line INS 1 cells (Beta-gene, Dallas, TX), and mouse pancreatic beta cell line MIN-6 cells, for example, to characterize the mechanisms of gene expression that are particular to that cell type. For example, α -TC1.6 cells express Nkx6.1 mRNA but do not express Nkx6.1 protein. In contrast, INS-1 cells express both Nkx6.1 mRNA and Nkx6.1 protein. Current evidence supports a role for RNA binding proteins in this restrictive expression during islet development.

In another embodiment, human preadipocytes or adipocytes are isolated from lean or obese patients and differential expression of RNA binding proteins is obtained by microarray analysis. These RNA binding protein genes and their gene products function in adipocyte differentiation, adipocyte function, insulin action, insulin resistance, obesity and glucose and lipid metabolic pathways, for example.

RIBOTRAP™

Whereas microarray analysis allows for the simultaneous analysis of the expression of RNA binding proteins, RIBOTRAP™ combines a biochemical and molecular biological approach for isolating, or “trapping”, an unknown RNA binding protein or set of RNA binding proteins that interact with an nucleic acid of interest. This involves several different approaches, including the use of 1) affinity-labeled or epitope-tagged RNA binding elements as affinity reagents for *in vitro* isolation of RNA binding proteins and 2) expression or transformation of an affinity-labeled or epitope-tagged mRNA in cell culture models for

isolation of RNA binding proteins bound to the tagged mRNA *in vivo*. RIBOTRAP™ is useful when it is necessary to first identify an RNA binding protein on a specific mRNA. RIBOTRAP™ methods are described in detail in Example 2.

Figure 1 illustrates an example of an *in vitro* RIBOTRAP™ method in which a
5 biotinylated mRNA attached to a streptavidin-agarose support is used to identify and isolate an RNA binding protein present in a cell extract, according to standard methods.

Figure 2 illustrates one embodiment of the invention, in which an mRNA or portion of a mRNA of interest, "RNA Y", is used as "bait" to trap a new RNA binding protein (hexagon). Preferably, RNA Y is first converted to a cDNA using standard molecular biology techniques
10 and is subsequently ligated at the 3' or 5' end to a DNA tag (dotted lines) that encodes a sequence that will bind a ligand (Protein "X"). The resulting fusion RNA is expressed in cells, where endogenous RNA binding proteins can bind and interact with RNA Y. The cells are then lysed and cell-free extracts are prepared and contacted with Protein X, which has been immobilized on a solid support. After incubation, Protein X and the attached RNA fusion molecule and its
15 associated RNA binding proteins are washed to remove residual cellular material. After washing, the newly isolated RNA binding proteins are removed from the RNA-protein complex and identified by protein microsequencing or Western blotting. Useful ligands include mRNP complex-specific antibodies or proteins (*e.g.*, obtained from a subject with an autoimmune disorder or cancer). The RNA binding protein is further tested for its ability to regulate the
20 translation of the protein encoded by RNAY, and is tested for validation as a drug target.

In an embodiment, an RNA binding protein is isolated by RIBOTRAP™ from a natural biological sample such as an islet, a pancreatic beta cell, an adipocyte, a preadipocyte, a skeletal muscle cell, a cardiac muscle cell, a hepatocyte, or a population of cells. The population of cells may contain a single cell type. Alternatively, the population of
25 cells may contain a mixture of different cell types from either primary or secondary cultures or from a complex tissue, such as an islet or tumor.

In one embodiment, the RNA binding protein is isolated from a cell sample in which the expression of a component of an mRNP complex, or precursor thereof, has been altered, *e.g.*, induced, inhibited, or over-expressed, *e.g.*, by introduction into the sample or other genetic
30 alteration or after treating the cell or tissue with an agent such as glucose, insulin, a beta-adrenergic agonist, insulin-like growth factor-1 (IGF-1), glucagon-like peptide-1 (GLP-1), fatty acid, peroxisome proliferator activated receptor (PPAR) ligands (*e.g.*

thiazolidinediones, fibrates, halogenated fatty acids, and tyrosine derivatives), insulin-like growth factor-2 (IGF-2), an RNAi against an RNA binding protein, an enhancer of RNA binding protein expression, a nucleic acid, a hormone, an antibody, an antibody fragment, an antigen, a cytokine, a growth factor, a pharmacological agent (*e.g.*, chemotherapeutic, carcinogenic), a chemical composition, a protein, a peptide, and/or a small molecule. Where the compound is a nucleic acid, the nucleic acid may be a DNA, RNA, a PNA, an antisense nucleic acid, a ribozyme, an RNAi, an miRNA, an ncRNA, an rRNA, an siRNA, an snRNA, an snoRNA, an stRNA, a tRNA, an aptamer, a decoy nucleic acid, or a competitor nucleic acid, for example. In one embodiment, the compound may alter the expression of an mRNP complex component through competitive binding. A compound may inhibit binding between two or more mRNP complex components, such as between an RNA binding protein and an RNA, between an RNA binding protein and an mRNP complex-associated protein, between an RNA and an mRNP complex-associated protein, or between two RNAs, RBPs, or mRNP complex-associated proteins, for example. In another embodiment, the cell sample is infected with a pathogen, such as a virus, bacteria, prion, fungus, parasite, or yeast, for example, to alter expression of one or more mRNP complex components. Introduction of a nucleic acid encoding one or more mRNP complex components may be achieved by infection, transformation, or other similar methods known in the art. In one embodiment, an expression vector expressing one or more components of an mRNP complex is transfected into a cell. Suitable vectors include, but are not limited to, recombinant vectors such as plasmid vectors or viral vectors. The nucleic acid encoding the component is preferably operatively linked to appropriate promoter and/or enhancer sequences for expression in the cell. In an embodiment of the invention, a specific cell type is engineered to contain a cell type-specific or inducible gene promoter that drives expression of an RNA binding protein.

Alternatively, a knock-out cell line or knock-out organism may be produced, which either does not express a component of an mRNP complex or expresses decreased levels of the component. Preferably, the knock-out cell line or knock-out organism does not express a particular RNA binding protein, mRNA, and/or mRNP complex-associated protein associated with the mRNP complex.

In a preferred embodiment, the nucleic acid encoding the mRNP complex component is tagged in order to facilitate the separation, and/or detection, and/or measurement of the components. Accessible epitopes may be used or, where the epitopes on the components are

inaccessible or obscured, epitope tags on ectopically expressed recombinant proteins may be used. Suitable tags include, but are not limited to, biotin, the MS2 protein binding site sequence the U1snRNA 70k binding site sequence, the U1snRNA A binding site sequence, the g10 binding site sequence (Novagen, Inc., Madison, WI), and FLAG-TAG® (Sigma Chemical, St. Louis, MO). For example, a cell is transfected with a vector directing the expression of a tagged RNA binding protein and a ligand, such as an antibody or antibody fragment, that is specific for the tag, is used to immunoprecipitate the tagged RNA binding protein with its associated mRNAs from a tissue extract containing the transformed cell.

The expression of one or more mRNP complex components may be altered by contacting or treating the cell sample with a known or test compound. The compound may be, but is not limited to, a protein, a nucleic acid, a peptide, an antibody, an antibody fragment, a small molecule, an enzyme, or agents such as glucose, insulin, a beta-adrenergic agonist, insulin-like growth factor-1 (IGF-1), glucagon-like peptide-1 (GLP-1), fatty acid, peroxisome proliferator activated receptor (PPAR) ligands (e.g. thiazolidinediones, fibrates, halogenated fatty acids, and tyrosine derivatives), insulin-like growth factor-2 (IGF-2), RNAi against a RNA binding protein, an enhancer of RNA binding protein expression, and/or a small molecule (e.g., a putative drug).

RASTM

Once partial sequence of the RNA binding protein is obtained, the corresponding gene may be identified from known databases of cDNA and genomic sequences or isolated from a cDNA or genomic library and sequenced according to art known methods. Preferably, the gene is isolated, the protein is expressed.

Once an RNA binding protein of interest is identified, an antibody is generated against the recombinant RNA binding protein using known techniques. The antibodies are then used to recover and confirm the identity of the endogenous RNA binding protein. Subsequently, the antibody can be used for the Ribonomic Analysis System (RASTM) whereby the mRNP complex containing the RNA binding protein is isolated and the subset of cellular RNAs that are associated with the mRNP complex and RNA binding protein are identified by microarray analysis, which is illustrated in Figure 3 and described in more detail below.

While any method for the isolation of an mRNP complex or its components may be used in the present invention, the methods described herein or in U.S. Patent No. 6,635,422 or disclosed in co-pending U.S. Application Nos. 10/238,306 and 10/309,788 are preferred. For

example, *in vivo* methods for isolating an mRNP complex involve contacting a biological sample that includes at least one mRNP complex with a ligand that specifically binds a component of the mRNP complex, such as an RNA binding protein. For example, the ligand may be an antibody, a nucleic acid, or any other compound or molecule that specifically binds the component of the complex.

In another embodiment, the mRNP complex is separated by binding the ligand (now bound to the mRNP complex) to a binding molecule that specifically binds the ligand. The binding molecule may bind the ligand directly (*e.g.*, a binding partner specific for the ligand), or may bind the ligand indirectly (*e.g.*, a binding partner specific for a tag on the ligand). Suitable binding molecules include, but are not limited to, protein A, protein G, and streptavidin. Binding molecules may also be obtained by using the serum of a subject suffering from a disorder such as an autoimmune disorder or cancer. In an embodiment, the ligand is an antibody that binds a component of the mRNP complex via its Fab region and a binding molecule binds the Fc region of the antibody.

In another embodiment, the binding molecule is attached to a solid support such as a bead, well, pin, plate, or column. Accordingly, the mRNP complex is attached to the support via the ligand and binding molecule. The mRNP complex may then be collected by removing it from the support (*e.g.*, by washing or eluting it from the support using suitable solvents and conditions that are known to a skilled artisan).

In certain embodiments, the mRNP complex is stabilized by cross-linking prior to binding the ligand thereto. Generally, cross-linking involves covalent binding (*e.g.*, covalently binding the components of the mRNP complex together). Cross-linking may be carried out by physical means (*e.g.*, by heat or ultraviolet radiation), or chemical means (*e.g.*, by contacting the complex with formaldehyde, paraformaldehyde, or other known cross-linking agents), methods of which are known to those skilled in the art. In another embodiment, the ligand is cross-linked to the mRNP complex after binding to the mRNP complex. In additional embodiments, the binding molecule is cross-linked to the ligand after binding to the ligand. In yet another embodiment, the binding molecule is cross-linked to the support.

The methods of the invention allow for the isolation and characterization of a plurality of mRNP complexes simultaneously (*e.g.*, "*en masse*"). For example, a biological sample is contacted with a plurality of ligands each specific for different mRNP complexes. A plurality of mRNP complexes from the sample bind the appropriate specific ligands. The plurality of mRNP

complexes are then separated using appropriate binding molecules, thereby isolating the plurality of mRNP complexes. The mRNP complexes and the mRNAs contained within the mRNP complexes are then characterized and/or identified by methods described herein and known in the art. Alternatively, the methods of the invention are carried out on a sample numerous times and the mRNP complexes are characterized and identified in a sequential fashion, with each iteration utilizing a different ligand.

Following isolation of an mRNP complex, the level of expression of at least one mRNA associated with the mRNP complex is determined. The collection of mRNAs, together with the RNA binding proteins, and mRNP complex-associated proteins on a particular mRNP complex provides a ribonomic profile, that is indicative of the gene expression of a subset of functionally related gene products. It will be appreciated that ribonomic profiles differ from cell to cell as described previously. Thus, a ribonomic profile for one cell type can be used as an identifier for that cell type and can be compared with ribonomic profiles of other cells.

Figure 4 illustrates an embodiment of the invention in which the RASTM technology is used in conjunction with a RIBOTRAPTM method to identify functionally and/or structurally related mRNAs associated with an mRNP complex. Figure 4 shows a comparison of the data obtained using traditional analysis of total RNA compared to the data obtained using RIBOTRAPTM to first isolate a particular RNA binding protein is followed by the use of RASTM to identify associated mRNAs. The use of RIBOTRAPTM and RASTM provides a more sensitive assay that is enriched for the subset of RNAs associated with a particular RNA binding protein and which are likely functionally related. By comparison, microarray analysis of total RNA does not provide the same level of sensitivity and functionality and provides a more complex data set.

Amplification of the mRNA isolated according to the methods of the invention and/or the cDNA obtained from the mRNA is not necessary or required by the present invention. However, the skilled artisan may choose to amplify the nucleic acid that is identified according to any of the numerous nucleic acid amplification methods that are well-known in the art (e.g., polymerase chain reaction (PCR), reverse transcriptase polymerase chain reaction (RT-PCR), quantitative real time polymerase chain reaction (QRT-PCR), rolling circle amplification (RCA), or strand displacement analysis (SDA)).

One goal of the RASTM assay is to identify mRNAs that encode proteins that have functional relationships. Among the related functions that are expected are a) involvement of encoded proteins in a common metabolic pathway, b) encoded proteins that are temporally co-

regulated, c) encoded proteins that are similarly localized in or on the cell, d) encoded proteins that play a role in forming or regulating a biological machine (*e.g.*, a ribosome). The identification of complex traits and phenotypes that result from the expression of a set of functionally-related proteins would include such processes as cognition, cell-specific activation, inflammation, or differentiation. While proteins known to be involved in these complex processes are known from other studies, the majority of the functions remain largely unknown. One of the values of the invention is for discovering a larger set of proteins involved in these processes that could serve as alternative drug targets or surrogate markers.

In addition, the subpopulation of mRNAs that are present in an mRNP complex can be identified and examined for the presence of common sequence elements, such as 5' or 3' untranslated regions, or common functional features. RASTM can then be used to identify the unique subsets of RNAs associated with those RNA binding proteins. Computational analysis of the primary sequence for identifying Untranslated Sequence Elements for Regulation Codes (USER codes) may be used alone or in combination with secondary structure analysis. In addition, the subpopulation of mRNAs can be examined for functional relationships. For example, each mRNA can be categorized by gene annotation and by known functions in functional genomics databases (*e.g.*, Locus Link (NCBI, Bethesda, MD), GO Database (Gene OntologyTM Consortium), Proteome BioKnowledge[®] Library (Incyte Genomics, Inc., Palo Alto CA)). For example, if the RNA binding protein or mRNP complex is involved in immune regulation, the other mRNAs found in the same mRNP complex can be analyzed for their role in immune regulation. However, the mRNA could be bound indirectly through a different RNA binding protein or RNA in the mRNP complex (*e.g.*, is assessed for the presence of the USER code element in its UTR that recognizes the RNA binding protein or other known binding sites for RNA binding proteins).

An exemplary technique for isolating functional clusters of mRNAs is *in vivo* RASTM, whereby the unique repertoire of mRNAs (defined herein as a "functional cluster") that is associated with a particular RNA binding protein *in vivo* is identified. Alternatively, *in vitro* RASTM may be used, wherein the RNA binding proteins and mRNAs are associated *in vitro* and analyzed. The *in vitro* technique is useful if, for example, the RIBOTRAPTM technique for isolating endogenous RNA:protein complexes is not feasible, for example due to ineffective affinity reagents for immunoprecipitation of the intact endogenous complex.

In vitro RASTM

Example 5 provides examples of methods for performing *in vitro* RASTM. Briefly, an RNA binding protein is cloned by polymerase chain reaction (PCR) and the sequence verified and expressed in *E. coli* as a glutathione S transferase (GST) fusion protein.

5 Following purification, the GST-RNA binding protein was attached to glutathione Sepharose beads and exposed to mRNA preparations to assess its ability to selectively retain discreet mRNA pools. Messenger RNA retained by an individual GST-RNA binding protein was profiled by combined microarray and QRT-PCR analyses, according to standard methods. Messenger RNA untranslated region (UTR) sequences are aligned to search for obvious
10 consensus elements in the retained mRNA pools, and a small number (*e.g.*, 5-10 UTRs) are initially evaluated to confirm direct binding by biotinylated oligonucleotide-affinity chromatography (as described for RIBOTRAPTM).

In general, two types of mRNA preparations are used, purified cytoplasmic RNA and cleared cytoplasmic lysates. Purified cytoplasmic RNA is used to directly identify mRNAs
15 that encode *cis* binding elements for the RNA binding protein. Cellular lysates containing both RNA and protein may have improved specificity of the RNA binding protein:RNA interaction, for example, due to the presence of auxiliary factors that modulate binding.

For additional glucose and/or lipid-regulated RNA binding proteins, comparisons are made between mRNA pools retained using purified RNA or cytoplasmic lysates (as
20 described for RASTM) prepared from cells or tissue treated with an agent such as glucose, insulin, a beta-adrenergic agonist, insulin-like growth factor-1 (IGF-1), glucagon-like peptide-1 (GLP-1), fatty acid, peroxisome proliferator activated receptor (PPAR) ligands (*e.g.* thiazolidinediones, fibrates, halogenated fatty acids, and tyrosine derivatives), insulin-like growth factor-2 (IGF-2), RNAi against a RNA binding protein, an enhancer of RNA
25 binding protein expression, and/or a small molecule (*i.e.*, a putative drug).

Example 6 describes an example of *in vitro* RASTM. In short, human PTB was cloned into a glutathione S transferase vector and recombinant protein (GST-PTB) was purified as known to those skilled in the art. GST-PTB was immobilized onto glutathione Sepharose beads and incubated with cleared cytoplasmic lysates or purified RNA prepared from
30 pancreatic beta cells. The matrix is washed thoroughly with binding buffer and RNAs bound to GST-PTB were purified. As a control, the same RNA preparations were incubated with a

glutathione bound matrix containing GST protein alone or another GST-RNA binding protein. The purified RNA from each column was identified by microarray analysis or QRT-PCR.

In vivo RASTM

5 In another embodiment of the invention, endogenous mRNP complexes from cells or tissue are profiled by immunoprecipitation of endogenous mRNP complexes from cell lysates and characterization of mRNA content. A binding partner (*e.g.*, an antibody) to an individual RNA binding protein or other mRNP complex component is used to isolate the mRNP complex and identify and characterize the associated mRNAs, *e.g.*, during any given
10 disease state or under certain experimental conditions. In contrast to the tagged RNA binding protein approach described for *in vitro* RASTM isolation of endogenous RNA binding protein complexes does not require transfection and selection of cell lines expressing tagged RNA binding proteins prior to analysis. However, *in vivo* RASTM analysis requires antibodies specific for individual RNA binding proteins or other mRNP complex component
15 that can immunoprecipitate intact endogenous mRNP complexes. Polyclonal anti-peptide and/or full-length protein antibodies, monoclonal antibodies, or recombinant antibody libraries specific for a mRNP complex component such as an RNA binding protein may be used. For example, a commercial antibody for the RNA binding protein PTB (Zymed, South San Francisco, CA) was used to effectively immunoprecipitate PTB-containing mRNP
20 complexes from INS-1 cells.

Antibodies and fragments thereof that bind to mRNP complexes are generated using methods that are well known in the art. Such antibodies may include, but are not limited to, polyclonal, monoclonal, chimeric, single chain, Fab fragments, and fragments produced by a λ expression library. Antibodies and fragments thereof may also be generated using antibody
25 phage expression display techniques, which are known in the art.

For the production of antibodies, various hosts including, but not limited to, goats, pigs, rabbits, rats, chickens, mice, and humans are immunized by injection with the mRNP complex or any fragment or component thereof that has immunogenic properties. Depending on the host species, an adjuvant is used to increase the immunological response. Such adjuvants include, but
30 are not limited to, Freund's, mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole

limpet hemocyanin, and dinitrophenol. Among adjuvants used in humans, Bacilli Calmette-Guerin and *Corynebacterium parvum* are preferable.

Monoclonal antibodies to the components of the mRNP complex are prepared using any technique that provides for the production of antibody molecules by a cultured cell line. These
5 include, but are not limited to, the hybridoma technique, the human B-cell hybridoma technique, and the EBV-hybridoma technique. Generally, an animal is immunized with the mRNP complex or immunogenic fragment(s) or conjugate(s) thereof. Lymphoid cells (*e.g.*, splenic lymphocytes) are then obtained from the immunized animal and fused with immortalized cells (*e.g.*, myeloma or heteromyeloma) to produce hybrid cells. The hybrid cells are screened to identify those that
10 produce the desired antibody.

Antibodies may also be produced by inducing *in vivo* production in the lymphocyte population or by screening immunoglobulin libraries or panels of highly specific binding reagents as is known in the art.

Antibody fragments that contain specific binding sites for mRNP complexes may also be
15 generated. For example, such fragments include, but are not limited to, the F(ab')₂ fragments that can be produced by pepsin digestion of the antibody molecule and the Fab fragments that can be generated by reducing the disulfide bridges of the F(ab')₂ fragments. Alternatively, Fab expression libraries are constructed to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity.

20 Various immunoassays are used to identify antibodies having the desired specificity for the mRNP complex. Numerous protocols for competitive binding or immunoradiometric assays using either polyclonal or monoclonal antibodies with established specificities are well known in the art. Such immunoassays typically involve the measurement of complex formation between the component of the mRNP complex and its specific antibody. An immunoassay utilizing
25 monoclonal antibodies reactive to two non-interfering epitopes is preferred, but a competitive binding assay may also be employed.

The antibodies may be conjugated to a support suitable for a diagnostic assay (*e.g.*, a solid support such as beads, plates, slides or wells formed from materials such as latex or polystyrene) in accordance with known techniques. Antibodies may likewise be conjugated to
30 detectable groups such as radiolabels (*e.g.*, ³⁵S, ¹²⁵I, ¹³¹I), enzyme labels (*e.g.*, horseradish peroxidase, alkaline phosphatase), and fluorescent labels (*e.g.*, fluorescein) in accordance with

known techniques. Such devices preferably include at least one reagent specific for detecting the binding between an antibody and the RNA binding protein. The reagents may also include ancillary agents such as buffering agents and protein stabilizing agents (*e.g.*, polysaccharides and the like). The device may further include, where necessary, agents for reducing background interference in a test, control reagents, apparatus for conducting a test, and the like. The device may be packaged in any suitable manner, typically with all elements in a single container, along with a sheet of printed instructions for carrying out the test.

In an embodiment, full-length RNA binding protein genes are amplified by PCR from appropriate cDNA libraries and cloned into expression vectors (*e.g.*, pGEX or pDEST17 6X-His) for bacterial expression, purification, and antibody production. Antibodies are affinity-purified, characterized, and optimized for immunoprecipitation of the protein and its associated RNA binding proteins or mRNP complex. The ability of the antibody to precipitate RNAs in general is determined by a rapid, high-throughput analysis using a 2100 BioAnalyzer (Agilent, Palo Alto, CA). Non-immune controls include previously characterized RNA binding protein antibodies are run in parallel as negative and positive controls, respectively. Specific antisera that are able to immunoprecipitate the RNA binding protein and/or mRNP complex are used for further analysis.

Optionally, more than one peptide antigen may be chosen based on analysis of the protein sequence using software for antigenic determination (Antheprot, Lyon, France; uses Parker and Wellington algorithms), followed by a Blast P search in NCBI to ensure that the designed peptide is not significantly homologous to another protein. Peptides are selected from regions thought to lie outside the RNA binding domain, to enrich for epitopes that are more likely to be exposed in the mRNP complex. In an embodiment, 15-25 amino acid peptides are synthesized according to standard methods and conjugation to Keyhole limpet hemocyanin (KLH), followed by immunization of rabbits for polyclonal antibody production.

RNA binding proteins or mRNP complexes may be immunoprecipitated as follows. In an embodiment, antibodies specific for a particular RNA binding protein /mRNP complex are pre-bound to protein A beads, blocked with bovine serum albumin and washed extensively. After a final wash in lysis buffer, cell extracts are added. Nuclei-free cytosolic extracts are prepared essentially as described from cells (or tissue) that have been exposed to various experimental conditions (*e.g.*, low and high glucose). Incubation times and

temperatures are optimized for each anti-RNA binding protein antibody. The complexes are washed under nuclease-free conditions. The antibody-mRNP complex is then disrupted with denaturing buffer RLT (Qiagen, Inc., Valencia, CA), containing guanidine thiocyanate, and mRNA purified using Qiagen RNA isolation column chromatography (Qiagen, Inc.,
5 Valencia, CA). The purified mRNA is then processed for microarray analysis, for example on human or rodent microarrays (depending on the cell or tissue source) comprised of features (*e.g.*, 10,000-40,000 genes) representing up-to-date genomic content (*e.g.*, Affymetrix, Santa Clara, CA; Agilent, Palo Alto, CA or MWG Biotech, Inc. High Point, NC). A gene observed at 'detectable' levels that is present in each of the experiments is
10 considered a component of mRNP complex to which it is associated and its relative fold-enrichment above a total RNA microarray analysis is determined. Routinely, genes expressed at a level above local background are considered members of that cluster. The presence of the candidate genes and their relative fold-enrichment over total RNA are verified and more accurately quantified by QRT-PCR using sequence-specific primers.

15 In an embodiment, the combination of the *in vitro* and *in vivo* RASTM based approaches may be used to map mRNP complex pools and accurately define the RNA content of selected mRNP complexes.

The multicomponent nature of mRNP complexes can interfere with efficient immunoprecipitation due to inaccessibility of reactive polypeptide epitopes. In the absence of
20 appropriate affinity reagents or when endogenous complexes cannot be isolated, mRNAs associated with individual RNA binding proteins in a cell are identified by using RNA binding proteins tagged with one of several generic epitopes such as, for example, Flag, AU1, or T7. The binding epitopes are expressed on the N- or C-terminus of the RNA binding protein and introduced into an appropriate cell line for expression. Pooled cell lines are generated by
25 selection (*e.g.*, in zeocin) and screened for stable expression of the tagged RNA binding proteins. Commercially available antibodies (*e.g.*, α -T7, Novagen, Madison, WI) are used to immunoprecipitate mRNP complexes from cells, for example, INS-1 cells following mock or glucose treatment. As a positive control, tagged poly A binding protein (PABP1), which is known to bind virtually all polyadenylated mRNAs, is constructed and transfected into INS-1
30 cells for parallel immunoprecipitation of mRNP complexes. Messenger RNA pools isolated following low and high glucose treatment of the individual INS-1 cell lines (pooled lines) are evaluated by microarray analysis and selective QRT-PCR confirmation. The use of a tagged-

RNA binding protein is advantageous in that the functional cluster associated with the tagged-RNA binding protein can be directly compared with that isolated using a commercially available monoclonal antibody to the RNA binding protein. This allows for validation of the endogenous RNA binding protein cluster as well as assessment of the mRNA binding characteristics of the tagged-RNA binding protein.

The mRNA pools were converted into amino allyl cDNAs and labeled with cyanine dyes for use as probes on microarrays. Aminoallyl cDNA (aa-cDNA) was synthesized from RNA preps based on modifications of protocols by DeRisi (www.microarray.org; "Reverse Transcription and aa-UTP Labeling of RNA") and TIGR (www.tigr.org; Protocol M005), as described in Example 1. Purified aa-cDNA was coupled to cyanine dyes (Amersham Biosciences; Piscataway, NJ; Catalog # PA23001 (Cy3) or PA25001 (Cy5)), purified, and analyzed as described in Example 1.

For each microarray, material from one Cy3 labeling and one Cy5 labeling reaction were pooled and dried in a speed vac. The pooled samples were then hybridized to the microarray and the slides processed according to the general guidelines suggested by the manufacturer (MWG Biotech; High Point, NC).

Microarrays were scanned using an Axon 4000B Scanner and GenePix version 4.0 software (Axon; Union City, CA) and the resulting image files were quantified as described in Example 1.

An isolated mRNP complex can be examined, in part to determine expression of its components as a whole, or broken down into its individual components. The mRNP complex can be separated from the ligand as a whole, or the mRNA can be separated from the ligand-mRNP complex, followed by separation of the RNA binding protein from the ligand. Alternatively, if the mRNA is bound to the ligand, the RNA binding protein can be separated from the ligand-mRNA complex, and the mRNA then separated from the ligand. Practitioners in the art are aware of standard methods of separating the components, including washing and chemical reactions. After separation, each component of an mRNP complex can be examined and their identity, quantity, or other identifying factors preferably recorded (*e.g.*, in a computer database) for future reference.

cDNAs or oligonucleotides can be used to identify complementary mRNAs on mRNP complexes partitioned according to methods disclosed herein. cDNA or oligonucleotide based

microarray grids can be used to identify mRNA subsets *en masse*. Each target nucleic acid examined on a microarray has a precise address that can be located, and the binding can be quantitated. Microarrays may be arranged in a commercially available substrate (e.g., paper, nitrocellulose, nylon, any other type of membrane filter, chip, such as a siliconized chip, glass
5 slide, silicone wafer, or any other suitable solid or flexible support). In addition, mRNAs in a sample can be identified based upon the stringency of binding and washing, a process known as "sequencing by hybridization", according to standard methods.

Alternative approaches for identifying, sequencing and/or otherwise characterizing the mRNAs in an mRNA subset include, but are not limited to, differential display, phage
10 display/analysis, Serial Analysis of Gene Expression (SAGE), and preparation of cDNA libraries from the mRNA preparation and sequencing of the members of the library.

Methods for DNA sequencing that are well known and generally available in the art may be used to practice any of the embodiments of the invention. The sequencing methods may employ such enzymes as the Klenow fragment of DNA polymerase I, SEQUENASE®
15 (U.S. Biochemical Corp, Cleveland, OH), Taq polymerase (Perkin Elmer, Boston, MA), thermostable T7 polymerase (Amersham, Chicago, IL), or combinations of polymerases and proofreading exonucleases such as those found in the Elongase® Amplification System marketed by Gibco BRL (Invitrogen™, Carlsbad, CA). Preferably, the process is automated with machines such as the Hamilton Micro Lab 2200 (Hamilton, Reno, NV), Peltier Thermal Cycler (PTC200)
20 (MJ Research, Watertown, MA) and the ABI Catalyst and 373 and 377 DNA Sequencers (Perkin Elmer, Shelton, CT).

In an embodiment, the methods of the invention are carried out on isolated nuclei from cells that are undergoing developmental or cell cycle changes or that have otherwise been subjected to a cellular or an environmental change, performing nuclear run-off assays according
25 to known techniques to obtain transcribing mRNAs, and comparing the transcribing mRNAs with the global mRNA levels isolated from mRNP complexes from the same cells using cDNA microarrays. These methods can distinguish transcriptional from post-transcriptional effects on steady state mRNA levels *en masse*. As opposed to a total RNA or a transcription profile that depicts RNA accumulation representing a steady-state level of mRNA, which is affected by
30 transcriptional and post-transcriptional events, the mRNAs detected by nuclear run-off experiments represent only the transcription of a gene before the influence of post-transcriptional

events. The microarrays representing mRNP complexes contain discrete and more limited subsets of mRNAs than the transcriptome or nuclear run-offs.

Other methods for characterizing and identifying mRNP complex components include standard laboratory techniques such as, but not limited to, RT-PCR, QRT-PCR, RNase
5 protection, Northern Blot analysis, Western blot analysis, macro- or micro-array analysis, *in situ* hybridization, immunofluorescence, radioimmunoassay, and immunoprecipitation. The results obtained from these methods are compared and contrasted in order to characterize further the functional relationships of the mRNA subsets and other mRNP components.

The present invention also provides diagnostic methods for assessing the cell types
10 present in a sample or a population of cells such as pancreatic beta cells, adipocytes, preadipocytes, hepatocytes, skeletal muscle, and cardiac muscle. Such analyses can distinguish one cell type from another, cell types of different differentiation states, or cells from one person from another person, for example, a person with a disease or increased risk of disease, from a normal person. The method involves isolating at least one mRNP complex and detecting the
15 expression of at least one component of the mRNP complex, wherein the at least one component is specific for a certain cell type, so that the detection of the expression of the component is indicative of the presence of the cell type in the population of cells. The component may be specific for a certain cell type within an entire sample (*e.g.*, tissue or organism) or within the population of cells. The sample or population of cells may be, for example, a tumor, a tissue, a
20 cultured cell, a body fluid, an organ, a cell extract or a cell lysate. The methods of the invention may also be used to determine the cell types present in a population of cells. Alternatively, cell type, as used herein, may also refer to a class of cells derived from a particular tissue, a particular species, a particular state of differentiation, a particular disease state, or a particular cell cycle.

Validation of Functional Role for Genes Encoding Components of mRNP Complexes

25 To confirm that a component identified in the an mRNP complex plays a direct role in the etiology of a disease or other phenotype, candidate target genes encoding that component are chosen for gene silencing studies (*e.g.*, using antisense nucleic acids, RNAi, ribozymes, and/or transgenic animals). Comparison of RNA from control RNAi-treated samples with RNA prepared from RNA binding protein RNAi-treated samples can provide quantitative differences
30 in gene expression. Differential expression of genes in samples isolated from RNA binding protein-specific RNAi-treated cells or tissues provides data on identification and quantitative

changes in expression due to inhibition of the specific RNA binding protein by RNAi. Genes whose expression patterns are altered as a result of down-regulation of the specific RNA binding protein would be tentatively considered as a member of that RNA binding protein ribonomic cluster.

5 For example, for each candidate therapeutic gene, one or more short DNA segments representing the coding sequence of that gene is individually cloned into a plasmid vector in the sense or antisense direction, downstream of an appropriate promoter, such as a U6 polymerase III promoter or RNase P RNA H1. Plasmid vectors may be constructed that contain two or more short DNA segments of one or more candidate therapeutic genes in the sense and antisense
10 directions, downstream of a U6 polymerase III promoter or RNase P RNA H1. Alternatively, one may construct an RNAi by annealing chemically synthesized complementary 22 bp RNAs (Dharmacon, Lafayette, CO).

Following transfection of the vector or double stranded RNA into cultured cells according to standard methods, phenotypic characteristics are evaluated to determine the effect
15 of inhibiting the expression of the candidate target gene(s). In addition, to the inhibition of gene expression at the RNA and protein levels is verified by standard methods, such as, for examples, Northern blots, QRT-PCR, Western blot, or other analytical assay, which may include time course experiments to demonstrate the efficacy and duration of inhibition for the individual genes, according to art known methods.

20 Transfections can result in transient expression for one to five days. Alternatively, vectors expressing RNAi can be stably expressed in cultured cells by co-transfection and selection with a dominant selectable marker, such as neomycin. As alternatives to the use of RNAi, traditional antisense DNA or vectors expressing dominant negative forms of targets of interest are used. Antisense and dominant negative genes are delivered by direct DNA
25 transfection or through the use of virus vectors including, but not limited to, retroviruses, adenoviruses, adeno-associated viruses, baculoviruses, poxviruses, and polyomaviruses. The biological system of study chosen to demonstrate the role of a gene in disease or cellular phenotype is based upon knowledge in the art of the biological system, including a cell culture or animal model system that mimics relevant biological features.

30 Figure 5 illustrates the steps involved in the implementation and validation of RASTM analysis.

Identification of Therapeutic Targets

The invention provides methods for identifying a therapeutic target by comparing the ribonomic profiles of a "test" cell sample (*e.g.*, a cell that has been treated with an agent or is derived from a diseased individual) to the ribonomic profiles of a control sample (*e.g.*, a cell that is untreated or derived from a non-diseased individual). A difference in the expression of a component of an mRNP complex between the two samples is indicative that the component is regulated by, or regulates, other components of the mRNP complex and that therefore it is a candidate therapeutic target (*e.g.*, for the up or down-regulation of that component or a component that it regulates). The therapeutic target may include, but is not limited to, any component of an mRNP complex, nucleic acid coding therefore, or gene product thereof. In an embodiment of the invention, the test cell sample is treated with a test compound and the control sample comprises cells that have not been treated with the test compound. In another embodiment, the test and control cell samples comprise cells at different stages in their growth cycle. In yet another embodiment, the test cell sample comprises a tumor cell or other diseased cell, and the control sample comprises a normal cell. Target identification includes methods known to practitioners in the art, such as, but not limited to, the use of screening libraries, peptide phage display, cDNA microchip array screening, and combinatorial chemistry techniques known to practitioners in the art. Once the mRNA or protein target has been identified, its role in a particular physiological pathway or process is assessed. For example, an mRNA or protein can be inhibited or overexpressed in a cell or organism according to standard methods. The effect of the under- or Over-expression can then be assessed by phenotypic analysis of the cell or organism. For example, RNAi may be used to knock out gene expression of the component. The gene expression of other components of the physiological pathway can be assessed, for example, using microarrays, in order to determine the regulatory effect of the altered target on other components of the process or pathway. A summary of the steps for target discovery is provided in Figure 5.

Identification of Therapeutics

In another aspect, the invention provides methods for assessing the efficacy of a test compound as a therapeutic. A cell sample is contacted with a test compound and a ribonomic profile of the cell sample comprising the expression of at least one gene product associated with at least one mRNP complex is prepared. The expression levels of the gene product(s) in the cell

sample are compared to the expression levels of the gene product(s) in a control sample (*e.g.*, a cell sample that is not contacted with a test compound). Identification of a difference in expression of the gene product between the treated and untreated cell samples is indicative that the test compound is a potential therapeutic. Test compounds may be, for example, nucleic acids, hormones, antibodies, antibody fragments, antigens, cytokines, growth factors, pharmacological agents (*e.g.*, chemotherapeutics, carcinogenics, or other cells), chemical compositions, proteins, peptides, and/or small molecules.

In various embodiments of the invention, the therapeutic may stabilize or destabilize the mRNA or the mRNP complex-associated protein. In another embodiment, the therapeutic may either inhibit or enhance translation of the mRNA, inhibit or accelerate transport of the mRNA or the mRNP complex-associated protein, inhibit the binding of the RNA binding protein to the mRNA, inhibit the binding of the RNA binding protein to the mRNP complex-associated protein, or inhibit the binding of the mRNA to the mRNP complex-associated protein, for example.

In another aspect, the invention provides methods for assessing toxicity, potential side effects, specificity or selectivity of a test compound, for example, by altering the concentrations or amounts of a test compound used to treat a cell sample.

In yet another aspect, the present invention provides methods for monitoring the efficacy of a therapeutic in a subject. In accordance with the invention, an effective amount of a therapeutic is administered to a subject. At least one mRNP complex is isolated from a cell sample from the subject, wherein altered expression of a gene product associated with the mRNP complex is altered by administration of the therapeutic. The expression of the gene product in the cell sample after administration of the therapeutic is compared to the expression of the gene product in a control sample (*e.g.*, a second cell sample obtained from the subject either prior to administration of the therapeutic or from a normal subject). The tests are repeated over a period of time to monitor the continued efficacy of the therapeutic. A difference in expression between the treated and the control cell samples is indicative of the efficacy of the therapeutic.

Therapeutics may target over- or under-expressed proteins involved in the etiology of a disease, disorder, or condition. Such over- or under-expression may result in destabilization or stabilization of RNA and/or inhibit or enhance translation of the substrate RNA.

Therapeutics that Destabilize mRNA

If a disease, condition or disorder is characterized by overexpression of a protein, a therapeutic for treatment of such a condition will reduce or eliminate expression of the protein by decreasing the stability of the RNA encoding the protein and/or by inhibiting the translation of the RNA. For example, since RNA binding proteins enhance the stability of short-lived mRNAs encoding protooncogenes, growth factors and cytokines that contribute to cell proliferation, inhibition of RNA binding protein production may alleviate diseases such as cancers or autoimmune diseases (*e.g.*, by decreasing tumor growth or inflammation, respectively). In addition, RNA binding protein overexpression in several human tumors correlates with resistance to chemotherapy and UV irradiation. Increased stability of c-fos, c-myc, cyclin B1 and other short-lived mRNAs in response to UV-irradiation or therapeutic drugs is well known. Accordingly, inhibition of RNA binding protein expression in these tumors destabilizes the mRNA in the tumors and, as a result, renders the tumors more responsive to cancer treatments.

In order to reduce overexpression or to cease expression of a protein of interest, the mRNA can be destabilized or its translation inhibited by administering an effective amount of a suitable test compound (*e.g.*, an RNA binding protein inhibitor) either *in vitro* or *in vivo*. The test compound may bind mRNA so as to inhibit RNA binding protein binding to the mRNA by binding to the RNA binding protein; bind to and destabilize the mRNP complex, and/or bind the mRNA so as to directly destabilize or inhibit the translation of the mRNA, and/or bind the RNA binding protein so as to inhibit the translation of the mRNA, for example. Compounds that bind to the mRNA but that do not stabilize the mRNA may inhibit the ability of an RNA binding protein to stabilize the mRNA or regulate translation of the mRNA. If the compound binds competitively with an RNA binding protein, the compound can decrease mRNA stability by inhibiting the RNA binding protein's ability to bind the mRNA.

Alternatively, the test compound may inhibit RNA binding protein expression or its mRNA expression.

Effective test compounds (*e.g.*, RNA binding protein inhibitors) can be readily determined by screening compounds for their ability to interfere with the production of RNA binding protein or their ability to inhibit the binding to, and/or stabilization or translation of, mRNA, for example, by methods described herein. Compounds that function by inhibiting RNA binding protein or mRNA production can be identified by exposing cells that express the RNA

binding protein or mRNA of interest and monitoring the levels of RNA binding protein or mRNA expressed, respectively. Compounds that function by inhibiting the stabilizing effect of an RNA binding protein and/or its ability to inhibit translation of an mRNA can be identified by combining RNA binding protein and an mRNA that would otherwise be stabilized, adding
5 compounds to be evaluated as RNA binding protein inhibitors, or compounds that enhance RNA binding protein to result in inhibition of translation and monitoring the binding affinity of RNA binding protein and the mRNA. Compounds that increase or decrease the binding affinity of RNA binding protein and the mRNA can be readily determined by art known methods.

Therapeutics that Stabilize mRNA

10 If a disease, condition or disorder is characterized by underexpression of an mRNA stabilizing protein or results from inhibited translation of the mRNA, a therapeutic for treatment of such a medical condition may operate by stabilizing the mRNA associated with the underexpressed protein and/or enhancing the translation of the mRNA. Accordingly, mRNA may be stabilized or its translation enhanced by administering an effective amount of a
15 compound, either *in vitro* or *in vivo*. The compound may possess a similar binding ability and stabilizing and/or translation enhancing effect as the RNA binding protein or, may promote the RNA binding protein's ability to stabilize and/or enhance the translation of the mRNA, and/or may promote the production of the RNA binding protein or the mRNA of the RNA binding protein of interest. Such a compound may be referred to as an RNA binding protein inducer and
20 may operate by interacting with the mRNA, the RNA binding protein or both. Alternatively, mRNA can be stabilized and/or its translation enhanced by administering an effective amount of a suitable RNA binding protein that possesses the necessary mRNA stabilizing and/or translation enhancing effect.

Compounds that increase RNA binding protein production can be identified by initially
25 exposing cells that express the RNA binding protein to potential inducers and, monitoring the levels of the RNA binding protein, in accordance with the methods described above. If the level of RNA binding protein expression increases, the compound is an RNA binding protein inducer. Compounds that inhibit RNA binding protein binding to mRNA, but which bind and stabilize and/or enhance translation of the mRNA, can be identified by methods disclosed herein. A
30 skilled practitioner may combine RNA binding protein and an mRNA, add a compound, and monitor the binding affinity of the RNA binding protein and the mRNA. Compounds that

increase or decrease the binding affinity of an RNA binding protein and the mRNA can be readily determined by evaluating the binding affinity of the RNA binding protein to the mRNA after exposure to the compound, as described herein. By monitoring the concentration of mRNA and/or translation of mRNA over time, those compounds that bind to the mRNA can then be
5 assayed for their ability to stabilize and/or enhance translation of the mRNA.

High Throughput Screening Methods for Libraries of Compounds

In an embodiment of the invention, high throughput screening assays and competitive binding assays are used to identify compounds that bind to an mRNP complex or component thereof from combinatorial libraries of compounds (*e.g.*, phage display peptide libraries, small
10 molecule libraries and oligonucleotide libraries).

In one embodiment, an mRNP component, catalytic or immunogenic fragment thereof, or oligopeptide thereof, can be used to screen libraries of compounds in any of a variety of drug screening techniques. An exemplary technique is described in published PCT application W084/03584, hereby incorporated by reference. The fragment employed in such screening can
15 be free in solution, affixed to a support, or located on a cell surface or intracellularly.

The SELEX method, described in U.S. Patent No. 5,270,163, is used to screen oligonucleotide libraries for compounds that have suitable binding properties. In accordance with the SELEX method, a candidate mixture of single stranded nucleic acids with regions of randomized sequence can be contacted with the mRNP complex. Those nucleic acids having an
20 increased affinity to the mRNP complex can be partitioned and amplified so as to yield a ligand enriched mixture.

Phage display technology is used to screen peptide phage display libraries to identify peptides that bind to an mRNP complex or component thereof. Methods for preparing libraries containing diverse populations of various types of molecules such as peptides, polypeptides,
25 proteins, and fragments thereof are known in the art. Phage display libraries are also commercially available.

A library of phage displaying potential binding peptides is incubated with an mRNP complex to select clones encoding recombinant peptides that specifically bind the mRNP complex or components thereof. After at least one round of biopanning (binding to the mRNP
30 complex), the phage DNA is amplified and sequenced, thereby providing the sequence for the

displayed binding peptides. Briefly, the target, an mRNP complex, can be coated overnight onto tissue culture plates and incubated in a humidified container. In a first round of panning, approximately 2×10^{11} phage can be incubated on the protein-coated plate for 60 minutes at room temperature while rocking gently. The plates are then washed using standard wash
5 solutions. The binding phage can then be collected and amplified following elution using the target protein. Secondary and tertiary pannings can be performed as necessary. Following the last screening, individual colonies of phage-infected bacteria can be picked at random, the phage DNA isolated and subjected to automated dideoxy sequencing. The sequence of the displayed peptides can be deduced from the DNA sequence.

10 The biological activity of compounds can be evaluated using *in vitro* assays known to those skilled in the art (*e.g.*, protein synthesis assays or tumor cell proliferation assays). Alternatively, the biological activity of the compounds is evaluated *in vivo*. Various compounds including antibodies, can bind to mRNP complexes and components thereof with varying effects on mRNA stability. The activity of the compounds once bound can be readily determined using
15 the assays described herein.

Binding assays include cell-free assays in which an RNA binding protein and an mRNA are incubated with a labeled test compound. Following incubation, the mRNA, free or bound to a test compound, can be separated from unbound test compound using any of a variety of techniques known in the art. The amount of test compound bound to an mRNP complex or
20 component thereof is then determined, using detection techniques known in the art.

Alternatively, the binding assay is a cell-free competition binding assay. In such assays, mRNA is incubated with labeled RNA binding protein. A test compound is added to the reaction and assayed for its ability to compete with the RNA binding protein for binding to the mRNA. Free labeled RNA binding protein can be separated from bound RNA binding protein. By
25 subsequently determining the amount of bound RNA binding protein, the ability of the test compound to compete for mRNA binding can be assessed. This assay can be formatted to facilitate screening of large numbers of test compounds by linking the RNA binding protein or the mRNA to a support so that it can be readily washed free of unbound reactants. A plastic support (*e.g.*, a plastic plate such as a 96 well dish or chip) is preferred. The RNA binding
30 protein and mRNA suitable for use in the cell-free assays described herein can be isolated from natural sources (*e.g.*, membrane preparations) or prepared recombinantly or chemically. The RNA binding protein can be prepared as a fusion protein using, for example, known recombinan

techniques. Preferred fusion proteins include, but are not limited to, a glutathione-S-transferase (GST) moiety, a green fluorescent protein (GFP) moiety that is useful for cellular localization studies or a His tag that is useful for affinity purification.

A competitive binding assay may also be cell-based. Accordingly, a compound,
5 preferably labeled, known to bind an mRNP complex or component thereof, is incubated with the mRNP complex or component thereof in the presence and absence of a test compound. By comparing the amount of known test compound associated with cells incubated in the presence of the test compound with that of cells incubated in the absence of the test compound, the
10 affinity of the test compound for the RNA binding protein, mRNA, and/or complex thereof can be determined. Cell proliferation can be monitored by measuring the uptake into cellular nucleic acids of labeled bases (e.g., radioactively, such as ^3H , ^{14}C , or ^{32}P ; fluorescently, such as
CYQUANT (Molecular Probes, Eugene, OR); or colorimetrically such as BrdU (Sigma, St. Louis, MO) or MTS (Promega, Madison, WI)) as known in the art. Cytosolic/cytoplasmic pH
15 determinations can be made with a digital imaging microscope using substrates such as bis(carboxyethyl)-carbonyl fluorescein (BCECF) (Molecular Probes, Inc., Eugene, Oregon).

Other types of assays that can be carried out to determine the effect of a test compound on RNA binding protein binding to mRNA include, but are not limited to, the Lewis Lung Carcinoma assay and extracellular migration assays such as the Boyden Chamber assay.

Accordingly, the methods permit the screening of compounds for their ability to
20 modulate the effect of an RNA binding protein on the binding of and stability of mRNA. Using the assays described herein, compounds capable of binding to mRNA and modulating the effects on those cellular bioactivities resulting from mRNA stability and correlated protein synthesis are identified. The compounds identified in accordance with the above assays are formulated as therapeutic compositions.

25 Diagnosing and Monitoring Disease

In another aspect, the invention provides methods for diagnosing a disease or risk of a disease related to glucose and/or lipid metabolism (e.g., obesity or diabetes) or cellular function. A ribonomic profile from a subject's cell sample is prepared and at least one mRNP complex is analyzed. The expression of at least one gene product, for which altered expression is indicative
30 of a disease or risk of disease, is determined. The gene product may be an RNA binding protein, an mRNA, an mRNP complex-associated protein or other gene product bound to or associated

with the mRNP complex. The expression of the gene product in the cell sample is compared to the expression of the gene product in a control sample. The control sample may be, for example, a sample of normal cells or a second cell sample from the subject. Alternatively, the control sample is a positive control, for example, from a diseased and/or normal individual. By
5 observing the relative expression of the gene product in the cell sample compared to the control sample, the presence of a disease or risk of disease can be determined.

In another aspect, the invention discloses a method for monitoring a disease state in a subject. At least one mRNP complex is isolated from a diseased subject's cell sample, wherein the mRNP complex has at least one gene product that is associated with the disease. The
10 expression of the gene product in the subject's cell sample is compared to the expression of the gene product in a control sample. The identification of a difference in the expression of the gene product in the diseased subject cell sample compared to the expression of the gene product in the control sample is indicative of a change in the disease state of the subject. For example, a decrease in the production of a tumor related antigen or its mRNA is indicative of decreased
15 tumor load or remission; by contrast, an increase in expression of the tumor antigen is indicative of aggressive tumor growth. Such monitoring during drug treatment provides information about the effectiveness of the subject's drug regimen, and may indicate when a particular regimen is not, or is no longer, effective for treating the disease or condition. The control sample may be, for example, a second cell sample from the subject, preferably, obtained when the subject is free
20 of one or more symptoms of the disease. Alternatively, the control sample is, for example, from a normal subject or other normal cell sample.

In summary, the present invention provides useful *in vivo* and *in vitro* methods for determining the ribonomic profile of a cell and detecting changes in the ribonomic profile. The invention has numerous uses, including, but not limited to, monitoring cell development or
25 growth, monitoring a cell state, and monitoring perturbations of a biological system such as disease, condition or disorder. The invention further provides methods for diagnosing a disease, condition, or disorder and determining appropriate treatment regimens. The invention also is useful for distinguishing ribonomic profiles among organisms such as plant, fungal, bacterial, viral, protozoan, or animal species.

30 The present invention can be used to discriminate between transcriptional and post-transcriptional contributions to gene expression and to track the movement of RNAs through mRNP complexes, including the interactions of combinations of proteins with RNAs in mRNP

complexes. Accordingly, the present invention can be used to study the regulation of RNA stability. The present invention can be used to investigate the activation of translation of mRNAs as single or multiple species by tracking the recruitment of mRNAs to active polysomes; measuring the sequential, ordered expression of mRNAs such as mRNAs that encode
5 transcription factors or RNA binding proteins, and measuring the simultaneous, coordinate expression of multiple mRNAs. The present invention can also be used to determine the transacting functions of RNAs themselves upon contacting other cellular components. These and numerous other uses will be made apparent to the skilled artisan upon study of the present specification and claims.

10 The following Examples are set forth to illustrate the present invention, and are not to be construed as limiting thereof.

Exemplification

Example 1: Target Discovery Using Ribonomic Profiles

The general steps required for target discovery using the methods of the invention are
15 summarized in Figure 5. Briefly, expression profiles for RNA binding proteins are generated to identify RNA binding proteins that have altered expression in different cell types, in a disease phenotype, or in response to certain stimuli, for example. Candidate RNA binding proteins may then be cloned and their cDNAs inserted into various bacterial and mammalian expression
20 vectors for production of recombinant RNA binding proteins and overexpression of RNA binding proteins, respectively. Recombinant or purified RNA binding proteins are then used to generate monoclonal or polyclonal antibodies for use in RASTM analysis performed on extracts from cells or tissues. Intact mRNP complexes associated with the differentially expressed RNA binding protein are then immunoprecipitated, for example, using antibodies to the RNA binding
25 protein. Once the mRNP complex is isolated, the other components of the mRNP complex, including RNAs and other mRNP complex associated proteins, are identified and compared and characterized. Differential expression of the other components of the mRNP complex is
determined in different cell types, in a disease phenotype, or in response to certain stimuli. Once differential expression is determined and candidate mRNP components are identified, their
biological role, *e.g.*, participation in a certain pathway or disease, is validated by inhibition and
30 overexpression studies. mRNP components that participate in a certain pathway are candidate therapeutic targets for diseases relating to aberrant regulation of that pathway.

Establishing Expression Profiles for RNA Binding Protein Genes

In one procedure for identifying candidate RNA binding proteins for further analysis, RNA binding protein expression profiles are generated in control or agent treated cell lines or tissues, and from normal and diseased human tissues. The agents used to treat the cells or tissues may include any agent that affects insulin action, insulin secretion glucose metabolism or lipid metabolism such as, adiponectin, leptin, resistin (or agents that act through the receptors for adiponectin, leptin, resistin), tumor necrosis factor-alpha, glucose, insulin, a beta-adrenergic agonist, insulin-like growth factor-1 (IGF-1), glucagon-like peptide-1 (GLP-1), fatty acid, peroxisome proliferator activated receptor (PPAR) ligands (e.g. thiazolidinediones, fibrates, halogenated fatty acids, and tyrosine derivatives), insulin-like growth factor-2 (IGF-2), RNAi against a RNA binding protein, an agent that enhances RNA binding protein expression and/or a small molecule (e.g., putative drug).

Initial tissue, disease, or agent screening of RNA binding protein gene expression can be accomplished by Quantitative Real Time PCR (QRT-PCR) using oligo dT-primers and commercially available RNA samples (Stratagene, Inc., La Jolla, CA; Ambion, Inc., Austin, TX; BD Biosciences Clontech, Palo Alto, CA). 10-100µg of cDNA is used to perform Quantitative PCR (Q-PCR) using SybrGreen (Molecular Probes, Inc., Eugene, OR) and gene specific PCR primers on a BioRad iCycler Quantitative PCR machine (Biorad, Hercules, CA) using protocols provided by the manufacturer. Experimental results are analyzed using the accompanying BioRad iCycler software. RNA levels for candidate RNA binding proteins are normalized to rRNA.

In addition to the above approaches, for rapid and comprehensive screening of tissues and cell lines, a RIBOCHIP™ array (Ribonomics, Inc., Durham, NC, designed and manufactured by MWG Biotech USA, Highpoint, NC) may be used. The RIBOCHIP™ contains 50-mer oligonucleotides corresponding to RNA binding protein genes in duplicate, non-contiguous positions, plus control genes, on glass slides. The nucleic acid sequences were compiled from a wide variety of public databases and search tools including GenBank (NCBI, Bethesda, MD), PubMed (NCBI, Bethesda, MD), SRS Evolution (LION Biosciences, Cambridge, MA), LocusLink (NCBI, Bethesda, MD), Protein FAMily database (pFAM, Washington University, St. Louis, MO); Wellcome Institute ; Sanger Institute (Hinxton, UK), GO Database (Gene Ontology™ Consortium, Gene Ontology: tool for the unification of biology. The Gene Ontology Consortium (2000) Nature Genet. 25: 25-29), Structural Classification of

Proteins (SCOP©), and Package (Medical Research Council, Cambridge, UK). A detailed method for microassay analysis on the RIBOCHIP™ and section of differentially expressed genes is described below.

5 The RNA binding proteins identified as having altered expression in response to treatments, disease, or cell cycle changes are useful for prioritizing candidates for RAS™. In addition, RNA binding proteins themselves may be candidates for therapeutic targeting and/or gene therapy (*i.e.*, gene replacement or gene silencing) or therapeutic antibody targets.

Cloning and Expression of RNA Binding Protein Genes in Bacterial Vectors

When candidate RNA binding proteins are identified, full length cDNA clones are
10 generated by reverse transcriptase-PCR (RT-PCR) using commercial RNA tissue sources and standard methods. For example, full-length plasmid clones are constructed based on phage lambda-based (att) site-specific recombination protocols (Invitrogen, Corp., Carlsbad, CA) for the GATEWAY™ pENTRD-Topo entry vectors and pDEST17 6XHis destination vectors (Invitrogen, Corp., Carlsbad, CA) or glutathione S transferase vectors (*e.g.*, pGEX from
15 Amersham, Piscataway, NJ). *Escherichia coli* (*e.g.*, BL21SI or BL21A1) expressing polyhistidine-tagged or GST-tagged RNA binding protein fusion proteins are grown to mid-log phase at 37°C and induced in 0.3 M NaCl for BL21SI cells or in 0.2 % mM arabinose or about 0.1mM to about 1mM IPTG for BL21A1 cells at 20-37°C for about 2-6 hours (specific time based upon optimization in pilot expression studies for each clone). Bacterial cells are lysed by
20 sonication and the RNA binding protein-fusion protein is purified on nickel columns (Qiagen, Inc., Valencia, CA) or glutathione Sepharose (Amersham, Piscataway, NJ) using standard methods. Insoluble fusion proteins are maintained and purified in the presence of 8M urea, and soluble proteins are maintained in phosphate buffered saline (PBS). The purified fusion proteins are used for immunization of mammals (*e.g.*, rabbits, pigs, or chickens) for production of
25 polyclonal antibodies using standard methods. Polyclonal antibodies are characterized by their ability to immunoprecipitate and detect by western blot, for example, native and recombinant proteins. The recombinant RNA binding protein is also used for *in vitro* RAS™ described below.

Analysis of Other mRNP Complex Components

Changes in the abundance or constellation of RNA binding proteins in a cell affect the processing of any mRNAs bound to those RNA binding proteins. The subset of mRNAs that are associated with an RNA binding protein is indicative of functional co-regulation that is critically
5 or causally involved in effecting a phenotypic change in the cell. Thus, those genes whose mRNAs are associated with tissue-, disease-, or agent altered mRNP complexes are a rich source of potential therapeutic targets.

RNA binding proteins that exhibit the most dramatic variation with regard to expression proceed into the next stage of analysis, the Ribonomic Analysis System (RASTM) assay
10 (Ribonomics, Durham, NC). The RASTM assay uses a microarray format to identify and/or quantify the specific mRNAs associated with particular RNA binding proteins. Commercially available glass slide arrays (such as, for example, Human Unigene 14K, Agilent, Palo Alto, CA and Pan Human 10K, MWG Biotech, Inc., High Point, NC), or membrane arrays, such as, for example, ATLASTM Arrays, BD Biosciences, Clontech, Palo Alto, CA), are employed using
15 protocols for hybridization, washing, and development provided by the array manufacturers.

The composition of RASTM assay lysis buffer (RLB) may vary, depending on the binding characteristics of a particular RNA binding protein. Basic RLB contains 50 mM HEPES, pH 7-7.4, 1% NP-40, 150 mM NaCl, 1 mM DTT, 100 U/ml RNase OUT (Gibco BRL, Invitrogen Corp., Carlsbad, CA), 0.2 mM PMSF (Sigman Aldrich, St. Louis, MO), 1 µg/ml aprotinin
20 (Sigman Aldrich, St. Louis, MO) and 1 µg/ml leupeptin (Sigman Aldrich, St. Louis, MO). Variations of these basic components included changes in salt concentrations (*e.g.*, about 0 to about 500 mM NaCl or about 0 to about 5 mM KCl), ionic conditions (about 0 to about 10 mM MgCl₂ or about 0 to about 20 mM EDTA), and reducing environment (about 0 to about 5 mM DTT). For example, in order to prepare cell extracts for examining the polypyrimidine tract
25 binding protein (PTB) mRNP complex, cultured cells are washed in ice-cold PBS and scraped directly into RLB containing 5 mM MgCl₂ and incubated on ice for 10 minutes followed by centrifugation at 3,700 xg for 10 minutes at 4 °C.

It is necessary in certain cases to crosslink the mRNP complex prior to isolation so that the RNA binding protein remains associated to its mRNAs. This is performed on cultured cells
30 as well as fresh tissue samples. The extent of crosslinking is titrated for each cell line or tissue and monitored based on the ability to immunoprecipitate mRNA in the complex. For example,

cultured cells or tissues are incubated in PBS containing about 0 to about 1% formaldehyde at room temperature for about 15 - 60 minutes. Crosslinking is then quenched by the addition of 1M Tris pH 8.0 to a final concentration of 250 mM Tris pH 8.0 and incubated further for an additional 20 minutes. The samples are then washed 3x in PBS containing 50 mM Tris pH 8.0.

- 5 For cultured cells, the cells are pelleted and resuspended in radioimmunoprecipitation (RIPA) buffer (50 mM Hepes, pH 7.4, 150 mM NaCl, 1% NP-40, 0.1% SDS, 0.5% deoxycholate (DOC) (Sigma-Aldrich, St. Louis, MO) and 100 U/ml RNase Out (Gibco BRL, Invitrogen Corp., Carlsbad, CA) to about 2 mg/ml final protein concentration. For tissues, the samples are resuspended in RIPA and homogenized with a polytron to disrupt the tissue. Following the
10 initial lysis, the samples are subjected to sonication with a probe sonicator (Branson 450, Branson Ultrasonics Corp., Danbury, CT) at output setting 6, two times for 20 seconds each. Between sonications the samples are allowed to cool on ice for 2 minutes. Lysates are then cleared by centrifugation at 3,700 x g for 15 minutes. The next stages include immunoprecipitation and RNA extraction.

15 *Immunoprecipitation of mRNP Complexes and RNA Extraction*

- On average, typical final protein concentrations for the cellular lysates are 2 mg/ml. Approximately 2 mg protein is used for each immunoprecipitation condition. Cleared cellular extracts are incubated with primary antibody (e.g., an anti-PTB (Zymed, South San Francisco, CA) is used at a final concentration of 10 µg/ml) or a control antibody at equal concentration
20 (e.g., pre-immune or IgG sera (Pierce Biotechnology, Rockford, IL) at final concentration of 10 µg/ml) for 2 hours at 4°C. A 25 µl aliquot of Protein A Trisacryl beads (Pierce Biotechnology, Rockford, IL) is added and the samples rotated for 1 hour at 4°C. The immune complex is then washed 6x in RLB buffer by adding 1 ml of RLB buffer followed by brief centrifugations in a microcentrifuge for 30 seconds at 5,000 rpm. After the final wash, 50 µl of RNA extraction
25 buffer from the PICOPURE™ RNA isolation kit (Arcturus, Inc., Mountain View, CA) is added to the beads, vortexed briefly and centrifuged to pellet the beads. The extracted RNA is purified following the PICOPURE™ protocol (Arcturus, Inc., Mountain View, CA). RNA present in the mRNP complex is then quantified using the RIBOGREEN™ assay (Molecular Probes, Inc., Eugene, OR).

Amplification of RNA for Microarray Analysis

Since mRNA isolated from mRNP complexes represents only a small subset of total RNA, isolated mRNA may be amplified prior to labeling. Message Amp™ (Ambion, Inc., Austin, TX) is used for RNA amplification according to the manufacturer's instructions. Two rounds of amplification are performed prior to labeling by random primer polymerization with Cy3 or Cy5-dUTP. Hybridization and washing are performed according to the microarray manufacturer's protocols and as described above. Microarray data acquisition and analysis are performed as described below.

Microarray Analysis

These methods are employed for analysis of RNA for ribonomic profiling with the RIBOCHIP™ as well as analysis on pan arrays with RNA extracted from the mRNP complexes to identify genes within a Ribonomics cluster.

RNA Preparation

The mRNA samples to be analyzed are prepared from various cell and tissue-types by RNA extraction with RNeasy™ (Qiagen, Inc.), quantified by absorbance (A_{260}), and stored at -80°C until use. Purified, Dnase I treated RNA was routinely analyzed using an Agilent 2100 Bioanalyzer. RNA was assessed for purity by examining electropherograms for the presence of broad peaks overlapping the 28S and 18S ribosomal RNA (rRNA) peaks. Broad peaks of this nature indicate contamination with genomic DNA. If such contamination was detected, the RNA was retreated with Dnase I and purified as described above. In addition, the relative abundance of 28S to 18S rRNA was determined to assess the quality of the RNA sample. Ratios greater than or equal to about 1.7 for 28S/18S rRNA indicate little or no degradation of the RNA and are acceptable for microarray analysis. Ratios less than about 1.7 indicate degraded RNA that is not acceptable for microarray analysis.

Synthesis of aminoallyl-UMP labeled cDNA

Aminoallyl cDNA was synthesized based on modifications of protocols by DeRisi (www.microarray.org; "Reverse Transcription and aa-UTP Labeling of RNA") and TIGR (www.tigr.org; Protocol M005). Briefly, total RNA (10 µg) was combined with 2 µl dT₁₈ (200 µM), 2 µl random decamer (1 mM stock), and diethyl pyrocarbonate (DEPC) treated water to a

final volume of 17.5 μ l. Primers were annealed to the RNA template by heating at 70 °C for 10 minutes and then cooling to room temperature or on ice. Aminoallyl cDNA was synthesized by addition of combining the above reaction with 6 μ l SuperScript II first strand buffer, 3 ml 0.1 M dithiothreitol, 0.6 ml 50X labeling mix (25 mM dATP, 25 mM dGTP, 25 mM dCTP, 15 mM dTTP, and 10 mM aminoallyl-dUTP (Sigma; St. Louis, MO; Catalog A0410)), 1 ml RNaseOUT (Invitrogen; Carlsbad, CA; Catalog 10777-019), and 1 ml SuperScript II (Invitrogen; Carlsbad, CA; Catalog 18064-022) followed by incubation for 3 to 24 hours at 42 °C. The RNA was hydrolyzed by addition of 10 μ l each 1 M NaOH and 0.5 M ethylenediamine tetraacetic acid followed by incubation for 15 minutes at 65 °C. The solution was neutralized by addition of 10 μ l of 1 M HCl. The aminoallyl-cDNA was purified using Qiagen QiaQuick PCR purification kit with the following modifications. The cDNA was mixed with 5x reaction volumes of the Qiagen supplied PB buffer and transferred to a QIAquick column. The column was placed in a collection tube and centrifuged for 1 minute at 13,000 rpm. The column was washed by addition of 750 μ l of phosphate wash buffer (prepared by mixing 0.5 mL 1 M KPO₄ (9.5 mL 1M K₂HPO₄ + 0.5 mL 1M KH₂PO₄), pH 8.5; 15.25 RNase free water; and 84.25 mL 95% ethanol) and centrifuging at 13,000 rpm. The wash step was repeated and the column centrifuged 1 minute at maximum speed to remove all traces of wash solution. The column was transferred to a clean collection tube and the aa-cDNA was eluted by addition of 30 μ l of phosphate elution buffer (prepared by mixing 0.5 mL 1 M KPO₄, pH 8.5; 15.25 RNase free water; and 84.25 mL 95% ethanol). The elution was repeated once and the sample was dried in a speed-vac.

Coupling of Cyanin Reactive Esters to aa-CDNA and Purification of Labeled cDNA

The purified aa-cDNA was coupled to cyanine dyes (Amersham Biosciences; Piscataway, NJ; Catalog # PA23001 (Cy3) or PA25001 (Cy5)); purified; and analyzed as described. Stock solutions of Cyanin3 and Cyanin5 reactive N-hydroxysuccinamide dye were prepared by dissolving one tube of reactive dye in 73 μ l of anhydrous DMSO. Reactive dye was coupled to aa-cDNA by addition of 4.5 μ l reactive DMSO dye solution to the aa-cDNA and incubating for 1 hour in the dark at room temperature. Following coupling, the dye-labeled cDNA was purified using standard QIAquick PCR cleanup kit methods and buffers. The labeling reactions were analyzed for incorporation according to the TIGR M005 protocol.

Hybridization and processing of Spotted Microarrays

Each spotted microarray is sufficient for analysis of two Cy-dye labeled samples, one labeled with Cy3 and one labeled with Cy5. For each microarray, material from one Cy3 labeling and one Cy5 labeling reaction were pooled and dried in a speed vac. The pooled
5 samples were then hybridized to the microarray and the slides processed according to the general guidelines suggested by the manufacturer (MWG Biotech, High Point, NC).

Microarray Data Extraction and Analysis

Figure 6 provides a flow chart of the data extraction and analysis using microarrays. Microarrays were scanned using an Axon 4000B Scanner and GenePix version 4.0 software
10 (Axon, Union City, CA). The resulting image files were quantified using BioDiscovery's Imagene software version 5.5 (El Segundo, CA) using standard background and spot finding settings. Two methods of data analysis were employed. The preferred method involved pre-processing the data using the BioConductor Suite (www.bioconductor.org; v 1.2) of microarray libraries for the R statistical environment (www.r-project.org; v 1.7.1). Preprocessing involved
15 background subtraction, application of intra-array Lowess intensity and location dependent normalization, and, in some cases, inter-array scaling using the MAD function of the BioConductor normalization library. The normalized intensity data was exported for further analysis in GeneSpring (Silicon Genetics; Redwood City, CA). Within GeneSpring, differentially expressed genes were identified based on ANOVA analysis (Welch's t-test for 2
20 conditions) and a suitable p-value threshold. Typically, a p-value of ≤ 0.05 was employed, although this value could be increased as necessary. Additionally, one or more of the available multiple testing corrections were applied to the data to reduce the occurrence of false positives. This was not always possible, particularly if the number of replicates available was too small. An alternative and less desirable method of data analysis was also employed occasionally. This
25 involved filtering the data based on background subtracted signal intensity (*e.g.* ≥ 500) and fold differential expression between the experimental and control samples (*e.g.* ≥ 2 fold differential from control). Routinely, genes expressed at a level above local background are considered members of that cluster. The presence of the candidate genes and their relative folds enrichment over total RNA is verified and more accurately quantified by a QRT-PCR using sequence-
30 specific primers.

In a standard RASTM analysis (e.g., comparing normal vs. disease cells or treated vs. untreated cells), quantitative and qualitative changes in the total RNA content are compared to changes in the RNA content of the particular mRNP complex. The data obtained is routinely grouped into four classes: (1) RNAs that show comparable quantitative changes in the mRNP complex, (2) RNAs present in the total RNA but not in the mRNP complex, (3) RNAs present in the mRNP complex but apparently absent or below the level of detection in total RNA, and (4) RNAs that change in the cluster in a quantitatively different manner than in the total RNA analysis. In addition, the RASTM assay identifies genes represented by class 4 that do not change in total abundance but that are repartitioned within the cell for alternative processing and regulation. As a result, different splice variants may be translated, the mRNA might be transported to and translated at a specific location within the cell, or translation itself might be up or down modulated. The subsets of genes identified within groups 3 and 4 cannot readily be identified by any other currently available approach to characterization of gene expression.

The methods of the invention identify genes that participate in the cellular pathways that contribute to the phenotypic changes associated with disease or certain cellular states and thus are attractive therapeutic targets. In addition, the methods of the invention identify target classes that have proven to be tractable targets for small molecule drugs. These target classes include nuclear receptors (e.g., hormone receptors), G-protein coupled receptors, phosphodiesterases, kinases, proteases, and ion channels, among others. Other target classes of therapeutic interest include secreted molecules, extracellular ligands, and phosphatases.

For RNA binding proteins identified or differentially expressed on the RIBOCHIPTM and for candidate target genes or gene products identified by the RASTM assay followed by global gene expression analysis on pan arrays, QRT-PCR was used to validate the expression at the RNA level when possible at the protein level by Western blot. For QRT-PCR, RNA is reverse transcribed to cDNA using Superscript II reverse transcriptase (Invitrogen, Carlsbad, CA, Cat# 18064-014) following the recommended kit protocol.

In 96 well PCR plates, 50ng of cDNA/well were incubated with 1X iQ sybr green supermix (Biorad, Hercules, CA. Cat# 94547) and either reaction specific or control primer pairs for a final volume of 50ul. All reactions were in duplicate. QRT-PCR reactions were run on a Biorad iCycler machine, using the sybr 2 step program (1 cycle at 95 C for 8minutes and 30 seconds; 40, 2 step cycles of 95 C for 30 seconds followed by 60 C for 60 seconds; 100 cycles of 55 C for 10 seconds). Data are compared to a normalized gene such as actin, GAPDH, or

ribosomal RNA. Differences in cycle time are used to compare and determine expression values relative to controls.

Immunoprecipitation of RNA Binding Protein Complexes

As an example of immunoprecipitation and isolation of a mRNP complex using RASTM,
5 the PTB ribonomic cluster (referred to also as PTB-cluster or PTB functional cluster) was isolated. In this example cell extracts were prepared from INS-1 cells (BetaGene, Inc., Dallas TX) that had been stepped-down in low glucose and then stimulated with high glucose media for 2 hours as described above. Cell extracts were prepared by harvesting in RLB buffer as above. Following centrifugation, the cell extracts were brought to 300mM NaCl and 15 mM EDTA
10 (RLB-NaCl/EDTA). The extracts (500ug protein) were incubated with 10ug α -PTB (Zymed, Cat# 32-4800) or 10ug of a control IgG (source, city, state) for 2 hours followed by a 1 hour incubation with 30 μ l of protein A sepharose. The immunoprecipitates were washed 6 times in RLB-NaCl/EDTA. Optimization of immunoprecipitation of other RNA binding protein and associated components would be required. In examples of optimization, pH, ionic conditions,
15 salt concentrations, reducing environment and incubation times can be varied.

RNA was extracted and purified from the immunoprecipitates using PicoPure RNA isolation kits (Arcturus). The purified RNA was quantified by RiboGreen (Molecular Probes) analysis and integrity of the samples was determined using a BioAnalyzer (Agilent). From these analyses approximately 25-30ng of nucleic acid was associated with the control IgG
20 immunoprecipitates. In contrast, approximately 200 – 900 ng of nucleic acid was immunoprecipitated by the PTB antibody. In order to obtain enough RNA for microarray studies, samples were subjected to two rounds of amplification using the MessageAmp kits and protocols (Ambion). Analysis of 10K Rat Pan Microarrays (MWG Ct#2250-000000) were performed as described for the RNA binding of protein arrays.

25 This analysis revealed a highly enriched (>5-fold) subset of approximately 450 genes. The normalized intensities of many of the genes were altered (>2-fold) in the clusters isolated from cells treated with 15mM glucose whereas the same genes in the total RNA analysis were unchanged. This suggests that glucose could regulate the appearance of many mRNAs into or out of the cluster. Numerous predicted genes were highly enriched in the PTB-cluster and the
30 presence of many of these was regulated by glucose. Included in this list are mRNAs for Glut2, glucokinase, phosphofructokinase, Kir6.2 (the ATP-sensitive K⁺-channel), SUR1 (sulfonylurea

receptor 1), L-type Ca²⁺-channels, acyl-coa carboxylase and preproinsulin. In addition, and importantly, approximately 10% of the 450 genes in the PTB cluster had normalized intensity values at or below detectable levels when analyzed by microarray analysis of total mRNA samples. Thus, the ability to isolate the PTB cluster, purify and identify its associated mRNAs
5 lead to the identification of very low abundant genes that most likely would have been missed or ignored in a normal array analysis. The ability to isolate the PTB cluster, enrich for a unique subset of genes, their regulated appearance in the cluster and identification of very low abundant genes supports the hypothesis regarding the role of RNA binding proteins in gene/protein expression and their utility for obtaining novel target and cellular pathway information.
10 Expression of all candidate mRNAs in an RNP complex chosen for further downstream analysis are verified at the mRNA level by QRT-PCR using gene specific primers.

Example 2: Identification and Immunoprecipitation of Preproinsulin RNA Binding Proteins Using RIBOTRAP™

An alternative method for purifying and identifying RNA binding proteins is the
15 RIBOTRAP™ assay (Ribonomics, Durham, NC). Two approaches for RIBOTRAP™ are described below. The first approach is an *in vitro* affinity-based assay using immobilized biotinylated oligonucleotides with sequences corresponding to RNA binding protein binding elements (Method 1). The second approach uses an affinity-tag placed on a full-length mRNA of interest or fragment of the mRNA of interest, which is expressed in a cell culture model and
20 isolated using immobilized antibodies against the tag (Method 2).

To summarize Method 1, a cDNA representing a nucleic acid of interest or a portion of a nucleic acid that encodes an RNA binding protein binding site (*e.g.*, a 5' or 3' UTR) is cloned using standard techniques into an expression vector possessing an appropriate mammalian cell promoter (*e.g.*, a CMV, SV40, or actin promoter), or alternatively an adenovirus or retrovirus
25 vector, and transfected into a compatible mammalian cell line. For the isolation of RNA binding proteins that participate in glucose and/or lipid metabolism, the cDNA may be expressed in a preadipocyte, adipocyte, or pancreatic beta cell line, for example. Following expression of the engineered cDNA, a cell extract is prepared that maintains the association between RNAs and their associated RNA binding proteins and mRNP complex-associated proteins, if present. The
30 mRNA encoded by the transfected cDNA is affinity purified using an affinity protein that is known to bind to it, preferably one that does not interfere with the binding of the mRNA to its

RNA binding protein(s). The affinity protein used may be linked to a solid matrix, such as agarose or Sepharose beads, and may be biotinylated or otherwise labeled (Method 1 below). Alternatively, the affinity protein may also be bound to the solid matrix indirectly via binding to an antibody that is bound to the solid matrix (Method 2 below). The affinity protein-matrix is
5 used to isolate the expressed RNA, along with the RNA binding proteins and/or mRNP complex-associated proteins that are associated with the mRNA *in vivo*. Variations on the two methods include chemical crosslinking of the mRNP complexes with formaldehyde or the use of an epitope tagged or beaded binding element or an epitope tagged mRNA of interest.

Proteins that are isolated in association with the mRNA of interest using the
10 RIBOTRAP™ assay are identified using standard proteomic methods. For example, Matrix Assisted Laser Desorption/Ionization - Time-of-Flight Mass Spectrometry (MALDI TOF) and Tandem Mass Spectrometry (or Mass Spectrometry/Mass Spectrometry (MS/MS)) are used to identify peptide sequences that can be subjected to database searches. Antibodies reactive with identified RNA binding proteins or mRNP complex-associated proteins are raised in mammals
15 according to standard methods.

Methods and Materials

Method 1: *In Vitro* Affinity-Based Assay Using Immobilized Biotinylated Oligonucleotides

Probes for affinity-purification of preproinsulin RNA binding proteins were synthesized and biotinylated with biotin-modified T (thymidine) by art known methods (*e.g.*, Ross *et al.*
20 (1997) Mol. Cell. Biol. 17:2158-65). The probes for purification of preproinsulin RNA binding proteins were the following: a) for 3'-UTR element one 5'-gaauaaaaccuuugaaagagcacuac-3', b) for 3'-UTR element two 5'-cccaccacuaccuguccacccucugcaaug-3', and c) for 5'-UTR element two 5'-agccctaagtgaccagctacagtcggaaccatcagcaagcaggtcattgtccaac-3'. In addition, a negative control biotinylated probe (scrambled sequence) was used as described to identify and eliminate
25 non-specific RNA binding proteins. The biotinylated probes were immobilized to streptavidin agarose (Pierce Biotechnology, Rockford, IL) or streptavidin magnetic beads (DynaL, Lake Success, NY) overnight in a 1M NaCl-containing buffer as described (Ross *et al.*, 1997). Beads were washed in high salt buffer to remove unbound probe, and then equilibrated in binding buffer. Cell extracts were prepared in RLB lysis buffer containing (50mM HEPES, pH 7.5,
30 0.5% NP-40, 150 mM NaCl, 1mM DTT, leupeptin 1ug/ml, aprotinin 1 ug/ml and PMSF, 10% glycerol, 200 units/ml RNase Out). The lysates are centrifuged at 10,000 xg for 5 minutes and

the supernatants (approx 1mg/ml protein concentration) used in binding studies. Extracts were incubated with immobilized biotinylated probes (1-5 mg of coupled probe) for 4-12 hours at 4 °C, washed, and proteins eluted in SDS-PAGE sample buffer. After separation by SDS-PAGE bands corresponding to proteins specifically bound to probes are identified by Western blotting or protein sequencing as previously described.

To specifically confirm binding of polypyrimidine tract binding protein (PTB) to the preproinsulin 3' UTR, eluted PTB was analyzed by Western blot using commercially available PTB antibody (Figure 7). Both recombinant PTB and native PTB derived from INS-1 cell lysates was evaluated for binding. Figure 7 illustrates that PTB binds to the 3'UTR of preproinsulin but not the 5'UTR of preproinsulin.

Figure 8 illustrates the current paradigm of glucose-regulated RNA binding protein binding of PTB (also referred to as RBP1) to the 3' UTR of the preproinsulin mRNA, as well as putative binding of other unidentified PTB proteins. The 5'-UTR of preproinsulin mRNA contains a secondary (stem-loop) structure ($\Delta G = -10.8$ kcal/mol) that is similar to structures found in other mRNAs that undergo regulation of biosynthesis at the translational level. Furthermore, the stem-loop structure is conserved in mammalian preproinsulin mRNAs. The 5'-UTR alone can function as a glucose and/or lipid response element. When both 5'- and 3'-UTRs are present, there is an even greater response to glucose. In addition, the glucose-stimulated translation is pancreatic beta cell-specific, since no glucose response is observed in non-beta cells. This strongly suggests the involvement of glucose and/or lipid regulated RNA binding proteins working via the 5'-UTR. Not to be limited to any particular theory, the data suggest a model in which at low or resting glucose levels, an RNA binding protein(s) is bound to the 5'-UTR of the preproinsulin mRNA and represses its translation. Increased nutrient concentrations (such as lipid and glucose) cause a change in the abundance or in the affinity of the RNA binding protein(s) for the preproinsulin 5'-UTR, thus relieving the repression and allowing enhanced translation of preproinsulin mRNA.

Method 2: Direct Affinity-Tagging Of mRNA With An RNA-Epitope

A direct affinity-tagging of mRNA with an RNA-epitope assay is described below. This method is based on antibody-recognition of a unique RNA stem loop structure. The well-characterized antibody α -g10 (*i.e.*, α -T7-tag) is raised against the N-terminus of a g10 fusion protein by standard methods. This antibody is used to screen a complex library of

degenerate RNAs (10^6 molecules) representing various stem loop structures. Following stringent washing conditions, a single 40 nucleotide RNA species is identified (D10) that was specifically recognized by α -g10. Upon further characterization, the D10 RNA is shown to mimic the peptide antigen; thus one can use the peptide for competition or elution. When the RNA-epitope is inserted into an mRNA, the RNA epitope-tagged mRNA can be specifically recovered from a mixture of total cellular mRNAs using α -g10. Furthermore, the antibody alone has no reactivity with total eukaryotic cellular mRNAs.

The D10 RNA-epitope tag is placed at the end of the 3'-UTR of the gene for Nkx6.1 and preproinsulin by methods well-known to the skilled artisan. This is accomplished by PCR cloning the tag into the full-length cDNAs for Nkx6.1 or preproinsulin (obtained by PCR cloning). These constructs are used for 1) generating *in vitro* transcripts for competition and affinity reagents, and 2) overexpression of Nkx6.1 or preproinsulin in a mammalian cell culture model followed by recovery of the RNA epitope-tagged mRNA from cell extracts with α -g10.

For the preproinsulin studies, the D10 RNA epitope-tagged preproinsulin cDNA as subcloned into pcDNA3.1neo and used to transfect MIN-6, α -TC1.6, and NIH3T3 cells. Transiently transfected cells as well as established stable transfectants (selected with Neo) are examined. Once expression of the tagged mRNA is confirmed by RT-PCR, extracts are prepared as described above from cells incubated in low or high glucose. Mock transfected cells are also examined.

Construction and transfection into the various cell-types of a D10 RNA epitope-tagged Nkx6.1 is performed in a similar manner. For analysis, the RNA epitope-tagged mRNAs are isolated from the extracts using immobilized α -g10. Proteins in these complexes are eluted with SDS-PAGE sample buffer or using antigenic peptide (NH_2 -MASMTGGQMGRC-COOH), which was previously shown to compete for the D10 epitope. A comparison of protein profiles obtained from the various cell extracts (including mock transfected cells) identifies unique protein bands. The eluted proteins are processed as described in Example 1 above to obtain peptide sequence. One variation on this procedure included D10-tagging of a fragment of the full-length mRNA (*e.g.*, the 5'- or 3'-UTR alone containing the D10 epitope).

A comparison of RNA binding protein expression profiles from α -TC1.6 cells, pancreatic beta cells (which express both homeodomain transcription factor Nkx6.1 mRNA

and protein), and NIH3T3 cells is performed to identify cell-type specific RNA binding proteins using RIBOMAP™. These RNA binding proteins represented candidate proteins that control Nkx6.1 expression.

5 RAS™ is then performed using antibodies to these candidate RNA binding proteins and the resulting functional clusters analyzed for Nkx6.1 mRNA expression. A functional cluster containing Nkx6.1 mRNA could contain other mRNAs that are coordinately regulated, and may code for proteins involved in development of the endocrine pancreas and/or pancreatic beta cell differentiation. Proteins that bind to the 5'-UTR of Nkx6.1 mRNA are also purified.

10 Specificity and Mapping of RNA Binding Protein Binding Elements

In order to verify potential RNA binding proteins and their binding specificity, competition experiments using immobilized binding sites (either biotinylated probes or D10 epitope-tagged probes generated by *in vitro* transcription) are performed. For example, the specific binding site is immobilized with either streptavidin agarose or α -g10 agarose and
15 incubated with cell extracts or a recombinant RNA binding protein according to art known methods. The binding reactions are carried out in the absence or presence of increasing concentrations of control or competing non-biotinylated or non-tagged probes (synthetic oligonucleotides or oligonucleotides generated by *in vitro* transcription, as described above). Binding is analyzed by 1) electrophoretic mobility shift assays as described in the art and/or
20 2) SDS-PAGE followed by Coomassie staining, to detect the presence or absence of RNA binding protein bands. RAS™ may also be performed as a third verification procedure. In this case antibodies raised against the RNA binding protein are used to immunoprecipitate complexes as described above and microarray analysis is performed to identify the associated mRNAs, one of which should be the original endogenous target mRNA.

25 **Example 3: Analysis of RNA Binding Protein Expression and Associated mRNAs in Human Adipocytes and Preadipocytes**

Adipocytes have long been considered a primary location for glucose disposal and energy storage in the form of triglycerides (fat). Adipocytes also comprise critical endocrine tissue that not only responds to insulin through glucose uptake and lipogenesis, but also synthesizes and
30 secretes a variety of signaling molecules involved in systemic energy homeostasis. An analysis

of RNA binding proteins and their associated mRNAs and mRNP complex-associated proteins and their role in gene expression in adipocytes provides a better understanding of adipocyte function and can identify targets for therapeutics that treat conditions associated with aberrant glucose or lipid metabolism. A flow chart for an exemplary adipocyte analysis is provided in
5 Figure 9.

RNA binding proteins that are enriched in mature adipocytes vs. preadipocytes in lean individuals (BMI < 24) were identified as follows. Briefly, human preadipocytes were harvested from elective liposuction from three lean individuals according to standard procedures. A portion of the preadipocytes were differentiated in culture to mature adipocytes (Zen-Bio,
10 Durham, NC). The expression pattern of RNA binding proteins in mature adipocytes was compared to the expression pattern of RNA binding proteins in preadipocytes using a RIBOCHIP™ V.1 array (MWG Biotech, High Point, NC) according to the methods described in Example 1. Figure 10 provides a list of the RNA binding proteins and corresponding genes that are differentially regulated in adipocytes vs. preadipocytes. In another experiment, the RNA
15 binding protein expression in preadipocytes from obese individuals was compared to expression in mature adipocytes in obese individuals. Preadipocytes and adipocytes were obtained from obese individuals as described above. RNA binding proteins were identified using RIBOCHIP™ analysis as described in Example 1. Figure 11 provides a list of 14 RNA binding proteins and their corresponding genes that were induced 2 fold or more in mature adipocytes
20 from obese individuals as compared to preadipocytes from obese individuals.

The effects of insulin or the beta 3 agonist, BRL-37344, on RNA binding protein expression in human mature adipocytes was also examined. Mature adipocytes from lean individuals were obtained as described above and either left untreated (basal) or treated with 100 nm insulin or 1µM BRL-37344 and RNA prepared from these cells (Zen-Bio, Durham, NC).
25 Differential expression of RNA binding proteins were identified using RIBOCHIP™ analysis as described above. Figure 12 provides a list of the RNA binding proteins and corresponding genes that are differentially regulated in response to treatment with BRC-37344. Figure 13 provides a list of the RNA binding proteins and corresponding genes that are differentially regulated in response to insulin.

30 In addition, the expression pattern of RNA binding proteins in mature adipocytes from three lean individuals was compared to the expression pattern of RNA binding proteins in mature adipocytes from three obese individuals (BMI > 30). Preadipocytes were obtained by elective

liposuction and cultured as described above. Adipocytes from obese individuals showed an altered pattern of RNA binding protein expression.

These data provide a refined list of candidate RNA binding proteins for further validation for participation in an adipocyte pathway, insulin production or insulin action, insulin resistance, a lipogenesis pathway, diabetes, obesity, and/or glucose and lipid metabolism pathway, or any pathway that participates in an aspect of glucose and lipid metabolism, and for the isolation of associated mRNP complex-associated proteins, and associated RNAs.

Example 4: Analysis of RNA Binding Protein Expression in Rat Pancreatic Beta Cells Treated with Glucose

The effect of glucose on RNA binding protein expression in rat pancreatic beta cells was examined. A derivative of the INS-1 rat pancreatic beta cell line, clone 832/13, was chosen because of its ability to mimic many of the normal functions of beta cells of pancreatic islets. Whereas INS-1 cells respond to glucose treatment with a 2-4 fold increase in insulin secretion, clone 832/13 is induced 8-13 fold by glucose treatment.

Briefly, 832/13 cells were grown RPMI containing 10% fetal bovin serum (Invitrogen, Corp., Carlsbad, CA) to near confluence, shifted to low glucose (3mM) for 1 hour, and treated for 2 hours with fresh medium containing 3mM or 15mM glucose. RNA was prepared and differential gene expression of the RNA binding proteins was determined using the RIBOCHIPTM as described above. Figure 14 provides a list of RNA binding proteins and their corresponding genes that displayed a 2-fold up- or down-regulation as a result of glucose treatment.

These data provide a refined list of candidate RNA binding proteins for further validation for participation in an adipocyte pathway, insulin production or insulin action, insulin resistance, a lipogenesis pathway, diabetes, obesity, and/or glucose and lipid metabolism pathway, or any pathway that participates in an aspect of glucose and lipid metabolism, and for the isolation of associated mRNP complex-associated proteins, and associated RNAs.

Example 5: Identification of Differentially Expressed RNA Binding Proteins in HepG2 Cells in Response to Peroxisome Proliferator Activated Receptor Ligands

The effects of peroxisome proliferator activated receptor (PPAR) ligands on human RNA binding protein expression was examined in the human hepatocyte cell line HepG2. Liver is a

major insulin target tissue and one of the PPAR receptors, PPAR γ , is thought to be the major biological target for a number of insulin sensitizing agents, including thiazolidinediones, L-tyrosine derivatives, halogenated fatty acids and prostaglandins. The compounds profiled include prostaglandin J2, perfluorooctanoic acid, 2-bromohexadecanoic acid, Ciglitazone, Troglitazone, GW-9662, MCC-555, Wyeth 14643, and Bezafibrate. Profiling the effects of these compounds using the RIBOCHIPTM was expected to reveal changes in regulatory genes important for the pharmacological and toxicological properties associated with these agents. Common themes or patterns in gene expression likely represent common pharmacology and toxicology while distinct gene expression changes elicited by individual compounds or subsets of compounds likely represent unique pharmacological or toxicological properties. The changes in gene expression identified in this manner are therefore attractive candidates for validation surrounding participation in the mechanism of insulin action and the pharmacological and toxicological properties of PPAR γ ligands.

Briefly, HepG2 cells (obtained from ATCC (www.atcc.org; catalog number HB-8065)) were maintained as recommended in Minimal Essential Medium (MEM) with 10% fetal bovine serum (FBS) supplemented with antibiotics in p150 plates at 37 °C, 5% CO₂. Cells were split 1:5 and fresh media added every 3 days. Cytotoxicity was assessed using the Alamar Blue-based CellTiterTM Blue Cell Viability Assay (Promega; Madison WI) to determine the viable cell fraction that remained following a 72 hour period. Cells (~8,000 cells/well) were plated in 96 well BioCoat collagen coated plates (Becton Dickinson; Bedford, MA) using standard media. This allowed untreated control samples (0.25% DMSO) to be in late log phase (~70% confluent) at completion of the study. Cells were then allowed to recover for 24 hours at 37 °C, 5% CO₂. A two (2) fold dilution series was prepared for each compound starting at 3.0 mM in MEM containing 0.1% BSA (instead of 10% FBS) but without phenol red or antibiotics. Following the cell recovery period, the media was removed and fresh media containing compound was added. Treatments were performed in triplicate for each compound at each dose. Cells were incubated with compound for 72 hours at 37 °C, 5% CO₂. The viable cell fraction remaining was determined by washing the wells with fresh media without indicator, lysis of the remaining live cells by addition of 0.9% Triton X-100 in water, and performing the Alamar Blue assay as described in the CellTiterTM Blue Cell Viability Assay product literature. The concentration resulting in 50% cell death relative to a vehicle only control following 72 hours of treatment (LD₅₀) was determined using Prism 4.0 (GraphPad; San Diego, CA) dose-response analysis.

RNA for microarray analysis was obtained from cells treated for 24 hours at the determined LD₅₀. Typically, $\sim 1.5 \times 10^6$ cells were plated in a p100 dish and allowed to settle for 24 hours by incubation at 37 °C, 5% CO₂ in MEM + 10% FBS without antibiotics. Old media was removed and fresh MEM + 0.1% BSA without antibiotics containing compound at LD₅₀ concentration and 0.25% DMSO was added to the flask. A vehicle only treatment was also performed. Duplicate treatments were performed for each compound as well as for vehicle only controls. The cells were incubated with compound for 24 hours at 37 °C, 5% CO₂ following which they were harvested by scraping (without trypsinisation) and centrifugation. The cells pellets were flash frozen and stored at -80 °C until ready for RNA extraction.

Total RNA was extracted and analyzed for using the RIBOCHIPTM as described in Example 1. ANOVA analysis (p-value ≤ 0.05) was used to identify genes that were differentially expressed for each treatment compared to a vehicle only control (0.25% DMSO). Figures 15-22 provide lists of RNA binding proteins and their corresponding genes that are differentially expressed in HepG2 cells treated with bezafibrate (Figure 15), Wyeth 14642 (Figure 16), troglitazone (Figure 17), MCC-555 (Figure 18), ciglitazone (Figure 19), 2-bromohexadecanoic acid (2-BHDA) (Figure 20), prostaglandin J2 (PJ2) (Figure 21), and perfluorooctanoic acid (PFOA) (Figure 22).

Example 6: *In Vitro* RASTM Identification Of mRNAs Associated With Polypyrimidine Tract Binding Protein Complexes Using the Purified Recombinant RNA Binding Protein

As an alternate approach to *in vivo* RASTM performed using antibodies against the endogenous RNA binding protein or epitope-tagged RNA binding proteins, an *in vitro* RASTM was used. In brief, cytoplasmic extracts from cells or tissues or purified RNA from cell or tissues is incubated with a purified recombinant RNA binding protein immobilized on a solid support. The example given below is an *in vitro* RASTM assay performed using GST-PTB and purified RNA or cytoplasmic extracts prepared from INS-1 cells.

Cloning and Expression of RNA Binding Protein Genes that Regulate Insulin

The human PTB cDNA was cloned into a pGEX4T vector, which contains a GST affinity tag, and expressed in *E. coli* cells. The GST-PTB fusion protein was purified from bacterial lysates using the GST affinity tag, as described above.

Isolation of RNAs that Bind to PTB *In Vitro*

INS-1 cells were cultured as described in Example 2. Cells were placed on ice, washed 3 times with ice cold PBS and lysed in 1ml/dish of lysis buffer (50mM Hepes, pH 7.2, 0.5% NP40, 150mM NaCl, 2mM MgCl₂, 5% glycerol, 1mM DTT, 10ug/ml Aprotinin, 1ug/ml Leupeptin, 0.2mg/ml PMSF and 200U/ml RNaseOUT (Invitrogen, Carlsbad, CA. Cat# 10777-019). Cytosolic fractions were isolated by centrifuging the lysates at 3700g for 10 minutes at 4 °C. The supernatant was transferred to a fresh tube and the NaCl concentration was raised to 300mM and EDTA added for a final concentration of 20mM. This sample was then centrifuged at 10000g for 10 minutes at 4 °C. The supernatant is considered the cytoplasmic extract containing mRNA. As an additional sample, RNA is also purified from these extracts using Qiagen kits as previously described.

The GST-PTB fusion protein was used to screen for mRNAs that bind to PTB. Briefly, the purified GST-PTB fusion protein was bound to a glutathione sepharose (Amersham, Uppsala, Sweden. Cat# 17-0756-01) support through the GST linkage according to standard methods.

Purified RNA or cytoplasmic lysates containing mRNA were incubated with the bead-bound GST-PTB fusion protein for 2 hours at 4°C. RNAs that bind to GST-PTB were retained on the beads. Ionic conditions for binding and washing were altered to select for high affinity binding of mRNAs to PTB or other RNA binding proteins, as described above. In this case, beads were washed 5 times with binding buffer (50mM Hepes, pH 7.2, 0.5% NP40, 300mM NaCl, 20mM EDTA, 2mM MgCl₂, 5% glycerol, 1mM DTT, 10ug/ml Aprotinin, 1ug/ml Leupeptin and 0.2mg/ml PMSF). After the final wash, the beads were resuspended in 350ul of RNAeasy mini prep buffer RLT and purified RNA using RNAeasy mini prep protocol (Qiagen, Valencia, CA. Cat# 74104). Alternatively, bound mRNAs are selectively eluted with 10mM glutathione (Sigma, St. Louis, MO), according to standard methods, which competes with GST to displace the mRNA-RNA binding protein complexes from the beads. Glutathione elution enables the selective elution of only those mRNAs that are bound to the RNA binding protein, and minimizes contamination with mRNAs that are non-specifically associated with the sepharose matrix. As a positive control, eluted mRNAs were enriched for the presence of preproinsulin mRNA, which was directly assessed using QRT-PCR, according to standard

methods. The eluted and purified RNAs are then identified by microarray analysis as described in Example 1. Figure 23 provides a list of genes bound to purified recombinant GST-PTB.

RASTM Performed With An Epitope-Tagged RNA Binding Protein Expressed In Cells Or Tissues

5 As an alternative approach to *in vivo* RASTM using antibodies against the endogenous RNA binding protein or to *in vitro* RASTM, epitope-tagged versions of RNA binding proteins are expressed in a cell or tissue of interest. For example, a T7-epitope tagged PTB (T7-PTB) is transfected and expressed in INS-1 cells. The addition of the epitope tags streamlines the ability to immunoprecipitate the RNP complexes from the cells, since under most circumstances the
10 epitope is not buried within the complex. Following stable selection of T7-PTB, mRNP complexes containing the T7-PTB are isolated from cell extracts using RLB buffer as described and the T7 monoclonal antibody (Novagen, Madison, WI). RNA is extracted and identified by microarray analysis as described.

 The combined *in vitro* and *in vivo* analysis of RNP complexes offers a powerful
15 approach to the study of post-transcriptional regulation. The comparative analysis identifies the set of genes being coordinately regulated in a variety of approaches. For the genes associate with PTB in INS-1 cells, these data provide a roadmap of the regulatory, metabolic, and signaling pathways that act in concert to orchestrate the proper production and secretion of insulin, for example. Analysis of dynamic changes in the PTB mRNP complex has lead to
20 the identification of novel diagnostic biomarkers and a collection of compelling therapeutic targets for modulating insulin production or other gene involved in glucose and/or lipid metabolism, insulin action, insulin resistance, diabetes and obesity.

Example 7. Validation of potential therapeutic targets and components of cellular pathways by RNAi-mediated silencing of genes

25 Once genes within a ribonomic cluster are identified, in order to validate them as a potential therapeutic target or to place them in cellular pathways, RNAi-mediated gene silencing was performed to verify their importance in the mRNP complex. SMARTPOOLTM designed siRNAs (Dharmacon (Lafayette, CO) were used, which containa mixture of siRNAs that specifically targeted a gene of interest, resulting in a greater than $\geq 50\%$ reduction in the target
30 mRNA within 24h post-transfection.

SMARTPOOL™ siRNAs the ion channel nucleic acids that had previously not been associated with glucose-stimulated insulin secretion, included CNCG (cat# M-003833-00-05), CaCNA2D1, KCNC3 (cat#M-003838-00-05), and KCNB2 (cat#M-003830-00-05). Transfection of each siRNA was performed in INS-1 cells that were plated in 24-well culture dishes, and incubated with fresh RPMI media containing 10% fetal bovine serum 90 minutes prior to transfection. TransitTKO transfection reagent (Dharmacon, Lafayette, CO), 2 µl, was incubated for 15 minute at room temperature with SMARTPOOL™ siRNAs at a concentration range to yield a final concentration of 1-50 nM siRNA on the cells. After a 24 hour incubation at 37°C, the cells were processed for total RNA isolation and glucose-stimulated insulin secretion. Expression of target genes in untreated, control transfected and sequence-specific siRNA-transfected cells was assessed by QRT-PCR and/or immunoblotting. For insulin secretion, cells were incubated for 60 minutes in serum-free media containing 3mM glucose. The media was then changed to fresh media containing either 3mM glucose or 15mM glucose and incubated for 120 minutes. Conditioned media from each sample was then used to determine the levels of secreted insulin using an insulin ELISA (Linco Research Products, St. Charles, MO Cat#EZHI-14K). Compared to cells transfected with the control siRNA, transfection of INS-1 cells with siRNA to PTB (Figure 24A), CNCG (Figure 24B), KCNC3 (Figure 24B), KCNB2 (Figure 24B) and CaCNA2D1 (Figure 24C) showed altered insulin secretion suggesting that these are involved in the insulin secretory pathway (Figure 19). In addition, extensive time course experiments, glucose dose response experiments, and experiments that determine the ability to respond to other secretagogues, such as sulfonylureas, GLP-1 and fatty acids, can be performed.

RNAi-mediated gene silencing of the two potassium channels KCNC3 and KCNB2 caused an extreme increase in basal insulin secretion levels, suggesting these channels play a functional role in the process. These two potassium channel proteins were not previously implicated in regulating insulin secretion or pancreatic beta cell function. This is significant, since the action of a class of diabetes drugs (sulfonylureas or gliburides like GLUCOVANCE) act by inhibiting a K⁺ channel on the pancreatic beta cell. This inhibition leads to membrane depolarization, which allows calcium to enter the cell and stimulate release of intracellular secretory granules filled with insulin. These drugs act by increasing overall and basal insulin secretion, thereby controlling high glucose levels (hyperglycemia).

These results suggest that there are additional K⁺ channels that may work in this process and provide candidate targets for new diabetes drugs.

It is notable that many of the ion channel proteins identified on the PTB cluster were not previously identified as participating in glucose and lipid metabolism. These proteins represent
5 targets for new therapeutics that may be used to regulate a pathway that participates in glucose and lipid metabolism or other pancreatic beta cell function. Figure 25 illustrates some of the known pathways that participate in insulin secretion in pancreatic beta cells, indicating some of the proteins encoded by mRNAs found on the PTB cluster.

Over-expression of Target Proteins

10 Alternatively, cells can be transfected with nucleic acids encoding target proteins or treated with a transcriptional enhancer for a gene encoding a target protein of interest, in order to overexpress a particular target protein identified by the methods of the invention. These systems would then be subject to biological assays (*e.g.*, glucose-stimulated insulin secretion) as described above.

15 **Example 8: RIBOTRAPTM Characterization of PTB on the 3'-UTR of Preproinsulin mRNA**

RIBOTRAPTM experiments were performed in order to characterize the effect of glucose on the binding of PTB to the 3'UTR of preproinsulin.

Preparation of Cell Extracts: INS-1 cells were incubated in RPMI media containing 0.5 mM
20 glucose for 2 hours. The cells were washed and the medium replaced with RPMI containing either 0.5 mM (low glucose) or 15 mM (high glucose) for various times up to 2 hours. The cells were washed with cold PBS and harvested in 1 mL RLB lysis buffer (50mM HEPES, pH 7.5, 0.5% NP-40, 150 mM NaCl, 1mM DTT, leupeptin 1µg/ml, aprotinin 1 µg/ml and PMSF, 10% glycerol, 200 units/ml RNase Out). The lysates were centrifuged at 10,000 x g for 5 minutes
25 and the supernatants (approx. 1mg/ml protein concentration) were used in binding studies.

RIBOTRAPTM Binding Study: A biotinylated RNA oligonucleotide probe specific for the 3'-UTR of preproinsulin, 5'-gccaccacuaccugaccacccucugcaaugaauaaaaccuuugaagagc-3', and a biotinylated control RNA oligonucleotide probe, 5'-
ugaaauacaagcucagcaccacuacacaagcuaccagauacaacaagaucacc-3' were prebound to

streptavidin agarose beads according to standard methods. For PTB binding, the salt concentration of INS-1 cell extracts was adjusted to 300 mM NaCl and 10-100 μ l cell extract was incubated with the biotinylated oligonucleotide probes (1-50 μ g) for 30 minutes to 12 hours. The beads were washed in RLB binding buffer (RLB/300mM NaCl) and bound protein eluted in SDS-PAGE sample buffer according to standard methods. Detection of bound PTB by immunoblotting was carried out using a monoclonal antibody against PTB (Zymed, South San Francisco, CA). Figure 26 shows the results of the immunoblot probed with the α -PTB monoclonal antibody, and indicates that glucose stimulates an acute but transient increase in PTB binding to the preproinsulin 3'-UTR. No binding was detected using the control RNA oligonucleotide.

Example 9: Identification of PTB Ribonomic Cluster using RASTM

The PTB ribonomic cluster was isolated and characterized using RASTM. Cell extracts were prepared from INS-1 cells that had been stepped-down in low glucose and then stimulated with high glucose media for 2 hours as described above in Examples 7 and 8. Cell extracts were prepared by harvesting cells in RLB buffer as described in Example 7. Following centrifugation, the salt concentration of the cell extracts was adjusted to 300 mM NaCl and 15 mM EDTA (RLB/NaCl/EDTA). These extracts (500 μ g protein) were incubated with 10 μ g of the anti-PTB monoclonal antibody α -PTB (Zymed, Cat# 32-4800, South San Francisco, CA) or 10 μ g of a control IgG (Pierce Biotechnology, Rockford, IL) for 2 hours, followed by a 1 hour incubation with 30 μ l of protein A sepharose (Pierce Biotechnology, Rockford, IL). The immunoprecipitates were washed 6 times in RLB/NaCl/EDTA. RNA was extracted and purified from the immunoprecipitates using PicoPure RNA isolation kits (Arcturus, Mountain View, CA). The purified RNA was quantified by RiboGreen analysis (Molecular Probes, Eugene, OR) and the integrity of the samples was determined using a BioAnalyzer (Agilent, Palo Alto, CA). From these analyses, approximately 25-30 ng of nucleic acid was associated with the control IgG immunoprecipitates. In contrast, approximately 200 – 900 ng of nucleic acid was immunoprecipitated by the PTB antibody. In order to obtain enough RNA for microarray studies, samples of approximately 500ng were subjected to two rounds of amplification using the MessageAmp kits and protocols (Ambion, Austin, TX) as described by the manufacturer. Microarray analysis was performed as described in Example 1.

For purposes of examining potential therapeutic targets from the PTB-cluster, genes with $\geq 5X$ enrichment compared to amplified total RNAs were sorted into the drug target classes and are listed in Figure 27.

Example 10: Use of RNAi-mediated Gene Silencing of RNA Binding Proteins to

5 **Characterize RBP Clusters**

RNAi was used to inhibit PTB expression and to examine the effect of RNAi-mediated down-regulation of PTB expression on the expression of several genes within the PTB-cluster. INS-1 cells were plated in 24-well culture dishes, and incubated with fresh RPMI media containing 10% fetal bovine serum. TransitTKO transfection reagent (Dharmacon, Lafayette, CO), 2 μ l, was incubated for 15 minute at room temperature with SmartPool™
10 siRNAs (Dharmacon, Lafayette, CO, Cat# M-003841-00-05) targeted specifically to PTB at a concentration range to yield a final concentration of 1-50 nM siRNA on the cells. After a 24 hour incubation at 37°C, total RNA was isolated and used in QR-TPCR analysis. Figure 28 illustrates the effect of PTB inhibition on the expression of PTB, preproinsulin, and nine
15 additional genes found within the PTB-cluster. As indicated in Figure 28A, there was an 80% reduction in PTB mRNA expression, confirming the action of the PTB specific RNAi. In addition, CACNA1S, CACNA2D1, Casr, C1c3, Kcnj6, AND Loc245960 and were significantly down-regulated as a result of PTB knockdown. Figure 28B illustrates genes whose expression was up-regulated as a result of PTB knockdown. This includes insulin, which is up-regulated 3-
20 fold.

Equivalents

The invention may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The foregoing embodiments are therefore to be considered in all respects illustrative rather than limiting on the invention described herein. Scope of the
25 invention is thus indicated by the appended claims rather than by the foregoing description, and all changes that come within the meaning and range of equivalency of the claims are intended to be embraced therein.

Incorporation by Reference

All publications and patent documents cited in this application are incorporated by reference in their entirety for all purposes to the same extent as if the contents of each individual publication or patent document was incorporated herein.

5

We claim:

1 1. A method of identifying a therapeutic target, the method comprising the steps of:

2 (a) measuring protein or RNA levels of at least one component of an isolated mRNA
3 ribonucleoprotein (mRNP) complex in a first sample enriched for a cell comprising a first
4 phenotype; and

5 (b) comparing the levels determined in step (a) to the levels of the protein or RNA levels
6 of the component in a second sample enriched for a cell comprising a second phenotype,

7 wherein if the levels of the component in the first sample are different from the levels of
8 the component in the second sample, the component, a nucleic acid that encodes the component,
9 or a protein encoded by the component is a potential therapeutic target for the treatment of a
10 disease.

1 2. The method of claim 1, wherein the cell comprising the first phenotype is selected from
2 the group consisting of a mature adipocyte, a preadipocyte, pancreatic beta cell, a hepatocyte, a
3 skeletal muscle cell, and a cardiac muscle cell.

1 3. The method of claim 1, wherein the cell comprising the first phenotype is a mature
2 adipocyte and the cell comprising the second phenotype is a preadipocyte.

1 4. The method of claim 1, wherein the first phenotype is a disease related to glucose or lipid
2 metabolism and the second phenotype is a normal phenotype.

1 5. The method of claim 1, wherein the first phenotype is selected from the group consisting
2 of obesity, diabetes, hypoglycemia, glucotoxicity, lipidtoxicity, insulin-resistance,
3 hyperlipidemia, and lipodystrophy.

1 6. The method of claim 1, wherein the component is selected from the group consisting of
2 an RNA binding protein, an RNA, and an mRNP-associated protein.

1 7. The method of claim 1, the method further comprising the step of:

2 (c) treating the sample in step (a) with an agent prior to measuring the protein or RNA
3 levels of the component, wherein the agent alters the levels of at least one component of a
4 glucose metabolic or a lipid metabolic pathway.

- 1 8. The method of claim 7, wherein the agent is selected from the group consisting of insulin,
2 glucose, insulin-like growth factor-1 (IGF-1), a β -adrenergic agonist, glucose, glucagon-like
3 peptide-1 (GLP-1), fatty acid, a peroxisome proliferator activated receptor (PPAR) ligand, and
4 insulin-like growth factor 2 (IGF-2).
- 1 9. The method of claim 7, wherein the agent is a test therapeutic.
- 1 10. The method of claim 7, wherein the agent is selected from the group consisting of a
2 nucleic acid, a protein, a peptide, or a small molecule.
- 1 11. The method of claim 1 or 7, further comprising the step of isolating the component, a
2 nucleic acid encoding the component, or a protein encoded by the component.
- 1 12. The method of claim 1, wherein the component is Polypyrimidine Tract Binding Protein.
- 1 13. The method of claim 1, wherein the RNA binding protein is selected from the group
2 consisting of the RNA binding proteins identified in Figure 10 to Figure 22.
- 1 14. The method of claim 1, wherein the component comprises a tag.
- 1 15. The method of claim 1, wherein the component is an mRNA that encodes a protein
2 selected from the group consisting of a kinase, a transporter, a phosphatase, channel protein, a
3 protease, a receptor, a transcription factor, and a transferase.
- 1 16. The method of claim 1, wherein the component is selected from the group consisting of
2 3-phosphoinositide dependent protein kinase-1, nuclear ubiquitous casein kinase 2, neural
3 receptor protein-tyrosine kinase, MAP-kinase activating death domain, AMP-activated protein
4 kinase beta-2 regulatory subunit, calcium/calmodulin-dependent protein kinase IV, Protein
5 kinase C beta, adenylate kinase 3, mitogen activated protein kinase kinase 5, 6-phosphofructo-2-
6 kinase/fructose-2,6-bisphosphatase 2, phosphatidylinositol 4-kinase, Glucokinase, glycogen
7 synthase kinase 3 beta, phosphorylase kinase (gamma 2, testis), protein tyrosine phosphatase
8 (non-receptor type 1), protein tyrosine phosphatase (non-receptor type 5), inositol
9 polyphosphate-5-phosphatase D, Protein tyrosine phosphatase (receptor-type, zeta polypeptide),
10 dual specificity phosphatase 6, protein tyrosine phosphatase (non-receptor type 12), glucose-6-
11 phosphatase (catalytic), 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase 2, proton gated
12 cation channel DRASIC, Sodium channel (nonvoltage-gated 1, alpha (epithelial)), calcium

13 channel (voltage-dependent, alpha2/delta subunit 1), Potassium inwardly-rectifying (channel,
14 subfamily J, member 6), potassium channel regulator 1, calcium channel (voltage-dependent, T
15 type, alpha 1G subunit), cyclic nucleotide-gated cation channel, amiloride-sensitive cation
16 channel 1, potassium inwardly-rectifying channel J14, potassium large conductance calcium-
17 activated channel (subfamily M, alpha member 1), potassium voltage gated channel (Shab-
18 related subfamily, member 2), potassium channel subunit (Slack), potassium intermediate/small
19 conductance calcium-activated channel (subfamily N, member 1), Sodium channel (voltage-
20 gated, type V, alpha polypeptide), amiloride-sensitive cation channel 2 (neuronal), potassium
21 channel (subfamily K, member 6 (TWIK-2)), cation-chloride cotransporter 6, solute carrier
22 family 21 (organic anion transporter, member 12), amino acid transporter system A2,
23 peptide/histidine transporter, choline transporter, solute carrier family 31 (copper transporters,
24 member 1), solute carrier family 13 (sodium-dependent dicarboxylate transporter), solute carrier
25 family 2 (facilitated glucose transporter, member 13), solute carrier family 12 (potassium-
26 chloride transporter, member 5), Solute carrier family 6 (neurotransmitter transporter, serotonin,
27 member 4), Solute carrier family 2 A2 (glucose transporter, type 2), carboxypeptidase D,
28 ubiquitin specific protease 2, mast cell protease 1, proprotein convertase subtilisin / kexin, type
29 7, laminin receptor 1 (67kD, ribosomal protein SA), protein tyrosine phosphatase (non-receptor
30 type 1), calcium-sensing receptor, neural receptor protein-tyrosine kinase, glutamate receptor
31 (metabotropic 4), nuclear receptor subfamily 4 (group A, member 2), Neuropeptide Y5 receptor,
32 protein tyrosine phosphatase (non-receptor type 5), insulin-like growth factor 1 receptor, Protein
33 tyrosine phosphatase (receptor-type, zeta polypeptide), nuclear receptor subfamily 4 (group A,
34 member 3), glutamate receptor (metabotropic 1), Tumor necrosis factor receptor superfamily
35 (member 1a), insulin receptor, gamma-aminobutyric acid receptor associated protein, protein
36 tyrosine phosphatase, non-receptor type 12, cholinergic receptor (nicotinic, beta polypeptide 1),
37 olfactory receptor (U131), Gamma-aminobutyric acid receptor beta 2, glial cell line derived
38 neurotrophic factor family receptor alpha 1, Glycine receptor beta, glutamate receptor interacting
39 protein 2, adenylate cyclase activating polypeptide 1 receptor 1, asialoglycoprotein receptor 2,
40 adenosine A3 receptor, Fibroblast growth factor receptor 1, nuclear receptor binding factor 2,
41 purinergic receptor P2Y (G-protein coupled 1), nuclear receptor subfamily 1 (group H, member
42 4), peroxisome proliferator activator receptor(gamma), 5 hydroxytryptamine (serotonin) receptor
43 4, retinoid X receptor gamma, insulin receptor-related receptor, putative N-acetyltransferase
44 Camello 4, lecithin-retinol acyltransferase, Phenylethanolamine N-methyltransferase,
45 fucosyltransferase 2, Sialyltransferase 8 (GT3 alpha 2,8-sialyltransferase) C, UDP-

46 glucuronosyltransferase, alpha 1,3-fucosyltransferase Fuc-T (similar to mouse Fut4),
47 diacylglycerol O-acyltransferase 1, signal transducer and activator of transcription 3, ISL1
48 transcription factor (LIM/homeodomain), and oligodendrocyte transcription factor 1.

1 17. The method of claim 16, wherein the protein is encoded by a gene selected from the
2 group consisting of CNCG, CACNA2D1, KCNC3, and KCNB2.

1 18. A method for identifying a therapeutic target for the treatment of aberrant glucose
2 metabolism or lipid metabolism, the method comprising the steps of:

3 (a) measuring RNA or protein levels of at least one component of an isolated mRNP
4 complex in a first cell sample; and

5 (b) comparing RNA or protein levels determined in step (a) to the RNA or protein levels
6 of the component from a second cell sample,

7 wherein if the levels of the component in the first sample are different from the levels of the
8 component in the second sample, the component, a nucleic acid that encodes the component, or a
9 protein encoded by the component is a potential therapeutic target for the treatment of the
10 disease.

1 19. The method of claim 18, wherein the first cell sample is from an individual at risk of
2 having a disease or who has a disease and the second cell sample is from a normal or healthy
3 individual.

1 20. A method for identifying a therapeutic target related to the treatment of a disease, the
2 method comprising the steps of:

3 (a) measuring RNA or protein levels of at least one component of an isolated mRNP
4 complex in a sample that has been treated with an agent that alters the expression of a component
5 of a glucose metabolic or lipid metabolic pathway; and

6 (b) comparing RNA or protein levels determined in step (a) to the RNA or protein levels
7 of the component in an untreated control sample,

8 wherein if the levels of the component in the first sample are different from the levels of the
9 component in the second sample, the component, a nucleic acid that encodes the component, or a

10 protein encoded by the component is a potential therapeutic target for the treatment of the
11 disease.

1 21. A method for identifying a gene or gene product involved in a physiological pathway in a
2 cell, the method comprising the steps of:

3 a. isolating an mRNP complex comprising at least one component that participates
4 in a physiological pathway;

5 b. identifying at least one additional component of the isolated mRNP complex,
6 wherein the additional component is also involved in a physiological pathway.

1 22. The method of claim 21, wherein the physiological pathway comprises a metabolic
2 pathway or a regulatory pathway.

1 23. The method of claim 21, further comprising the step of confirming the activity of the
2 additional component by inhibiting the expression of the additional component in a cell and
3 determining the effect of the inhibition on metabolism.

1 24. The method of claim 23, wherein the inhibition step comprises inhibiting gene expression
2 of the additional component using an agent selected from the group consisting of an RNAi, an
3 antisense RNA, a ribozyme, and a PNA.

1 25. A method for identifying an agent that alters a physiological pathway, the method
2 comprising the steps of:

3 a. subjecting a cell sample to an agent;

4 b. isolating an mRNP complex comprising at least one component that participates
5 in a physiological pathway from the sample;

6 c. measuring the RNA or protein levels of at least one component of the isolated
7 mRNP complex,

8 d. comparing the RNA or protein levels of step (c) to the RNA or protein levels of
9 the component isolated from an untreated control sample,

10 wherein differential expression of the component in the agent-treated sample compared to the
11 untreated control sample is indicative that the agent regulates the physiological pathway.

1 26. The method of claim 25, wherein the agent interacts with or regulates a component of the
2 physiological pathway.

1 27. The method of claim 25, wherein the agent inhibits a physiological pathway.

1 28. The method of claim 25, wherein the agent enhances a physiological pathway.

1 29. The method of claim 25, wherein the physiological pathway is an insulin production
2 pathway or a lipogenesis pathway.

1 30. A method for identifying a protein that regulates glucose metabolism, the method
2 comprising the steps of:

3 a. measuring the expression in an isolated mRNP complex of at least one gene
4 product of a cell involved in glucose metabolism, wherein the gene product is selected from the
5 group consisting of an RNA binding protein, an mRNA associated with said RNA binding
6 protein, or an mRNP complex-associated protein;

7 b. treating the cell with an agent selected from the group consisting of insulin,
8 glucose, insulin-like growth factor-1 (IGF-1), a β -adrenergic agonist, glucose, glucagon-like
9 peptide-1 (GLP-1), fatty acid, a peroxisome proliferator activated receptor (PPAR) ligand, and
10 insulin-like growth factor 2 (IGF-2); and

11 c. measuring the expression of the gene product after treatment, wherein a
12 difference in expression of the gene product after treatment compared to expression of the gene
13 product before treatment is indicative that the protein regulates glucose metabolism.

1 31. A method for identifying an agent that regulates insulin production, the method
2 comprising the steps of:

3 a. contacting a cell involved in insulin production with a nucleic acid capable of
4 binding to at least one protein, wherein the protein is capable of binding to a 3' untranslated
5 region or a 5' untranslated region of a preproinsulin mRNA;

- 6 b. separating the nucleic acid from the protein; and
- 7 c. identifying the protein.

1 32. The method of claim 31, wherein the protein binds to a nucleic acid comprising a
2 sequence selected from the group consisting of 5'-gaauaaaaccuuugaaagagcacuac-3', 5'-
3 cccaccacuaccuguccaccccucugcaaug-3', and 5'-
4 agccctaagtgaccagctacagtcggaacctcagcaagcaggtcattgtccaac-3'.

1 33. An mRNP complex-associated with at least one of glucose or lipid metabolism, wherein
2 the mRNP complex comprises a polypyrimidine tract binding (PTB) protein, and at least one
3 mRNA associated with the polypyrimidine tract binding protein.

1 34. A method for identifying a component of an mRNP complex, the method comprising the
2 steps of:

- 3 (a) transfecting a cell sample with a nucleic acid that inhibits the expression of an RNA
4 binding protein;
- 5 (b) isolating total RNA from the cell sample and from a control sample;
- 6 (c) identifying RNAs that have altered expression in the nucleic acid-transfected sample
7 compared to the control sample.

1 35. The method of any one of claims 1, 7, 18, and 20, wherein the disease is related to
2 aberrant glucose or lipid metabolism.

1 36. The method of claim 21 or 25, wherein the physiological pathway comprises a glucose or
2 lipid metabolic pathway.

1 37. The method of any one of claims 1, 17, 20, 25, and 30, wherein at least one of said
2 measuring and said comparing steps comprises the use of an array.

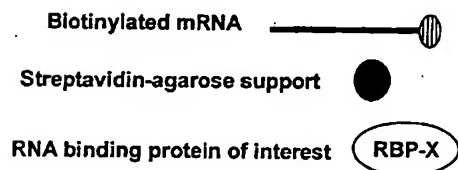
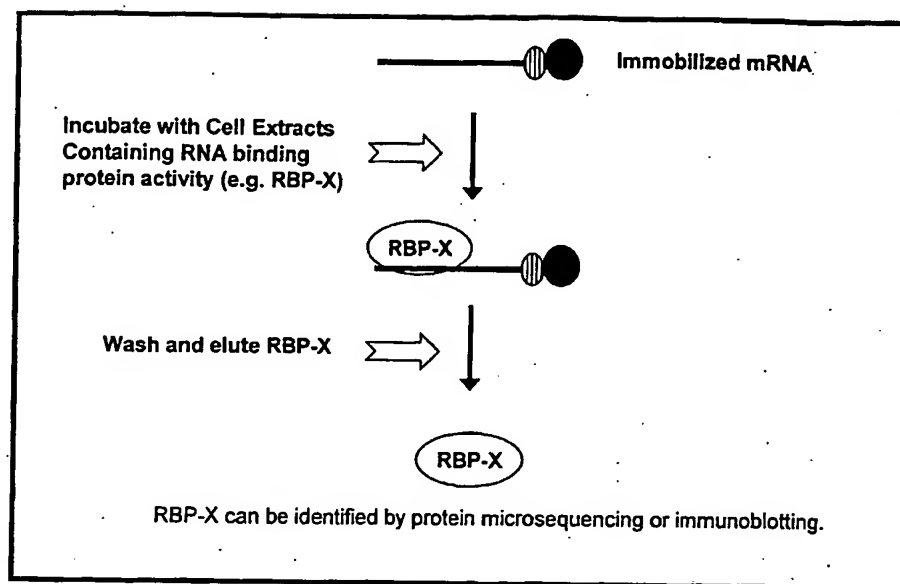


Figure 1

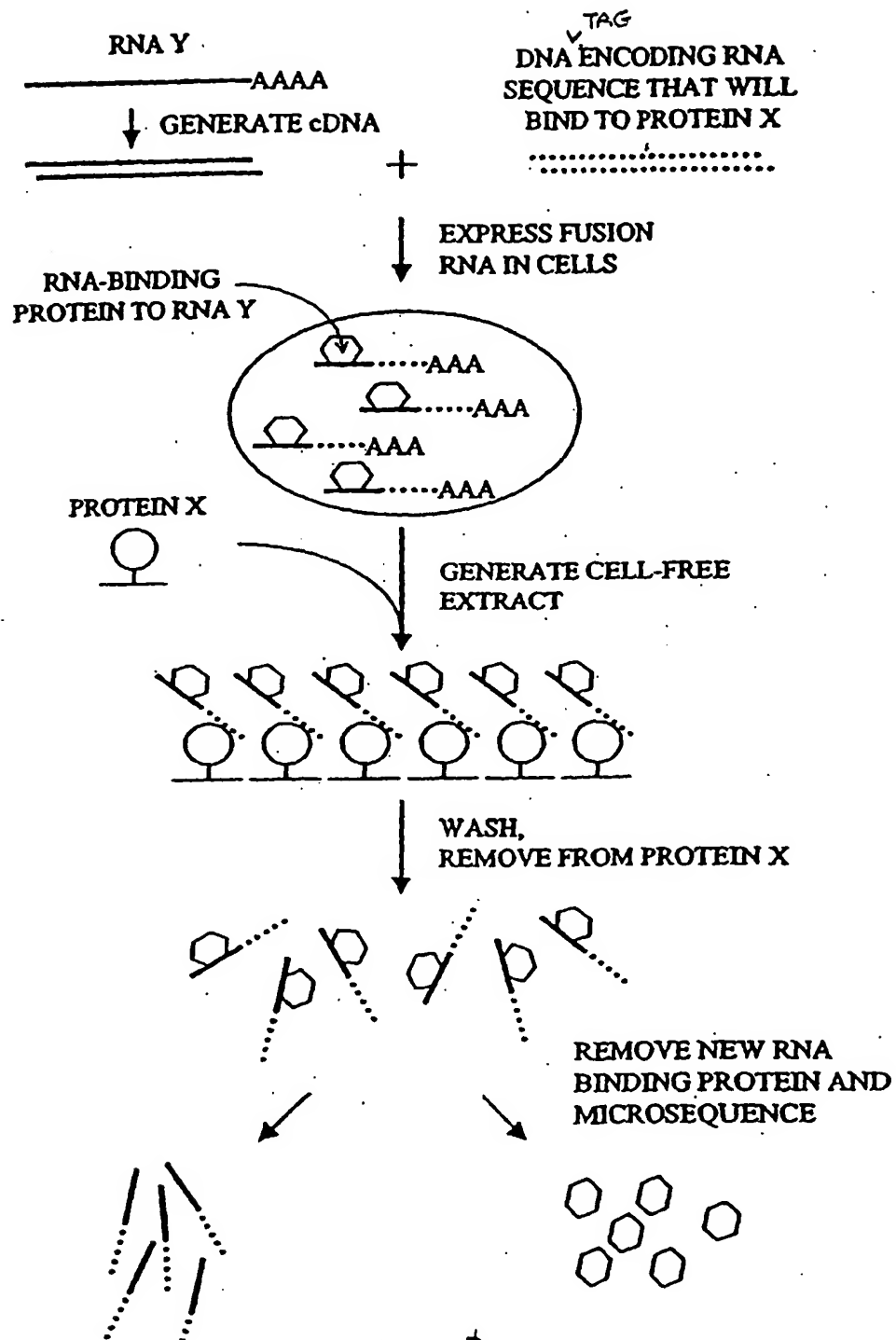


Figure 2

Ribonome

The Ribonome is the entire collection of RNAs and their associated RNA binding proteins (RBPs).

Ribonomic Clusters

RAS™ segregates the ribonome into distinct ribonomic 'clusters' based upon a specific RBP. Genes within each cluster are identified by microarray.

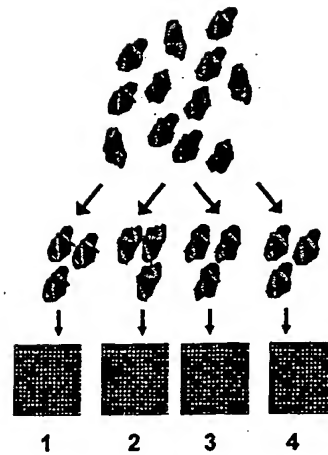


Figure 3

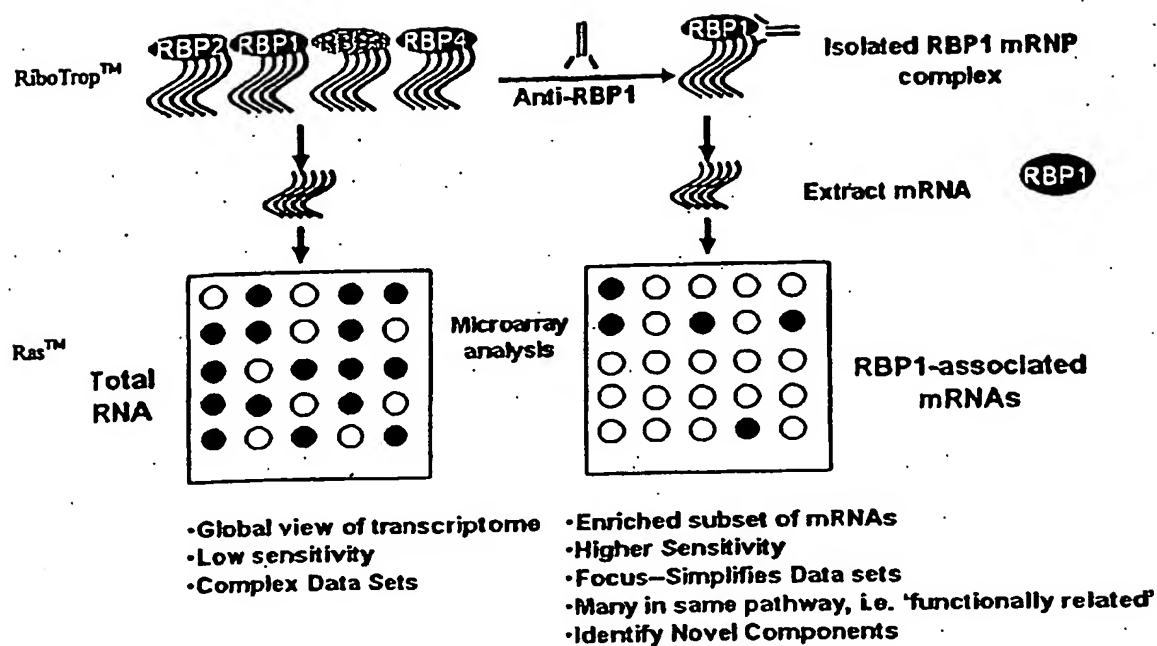


Figure 4

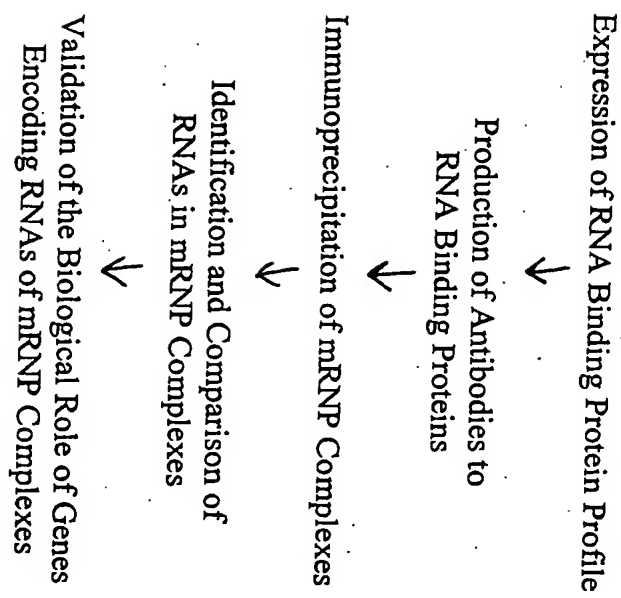


Figure 5

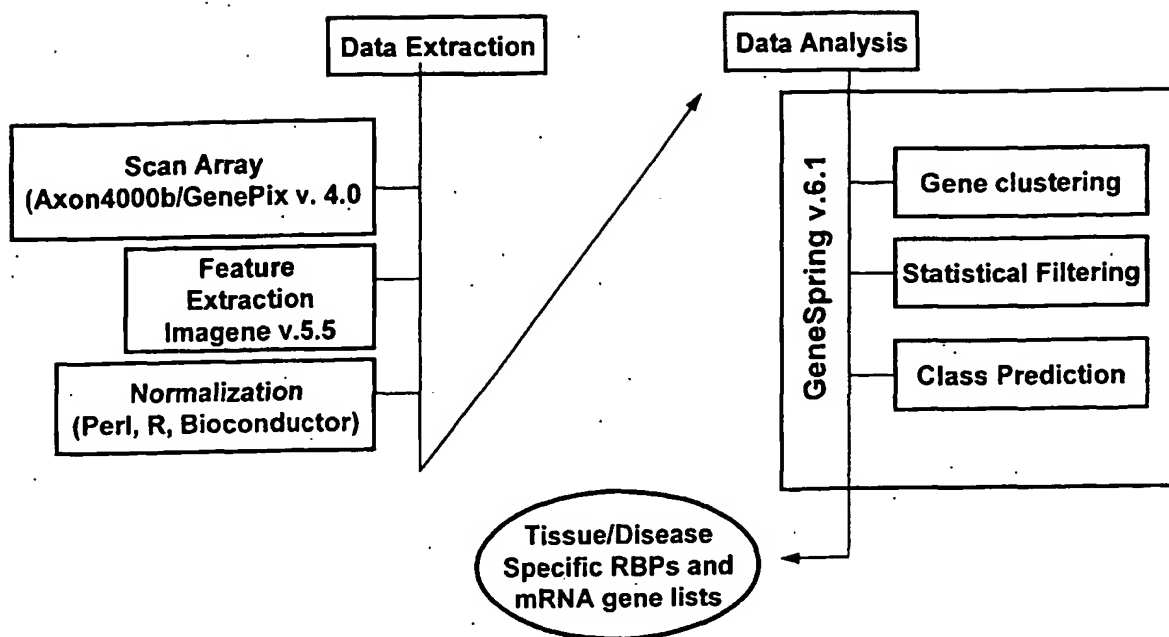


Figure 6:

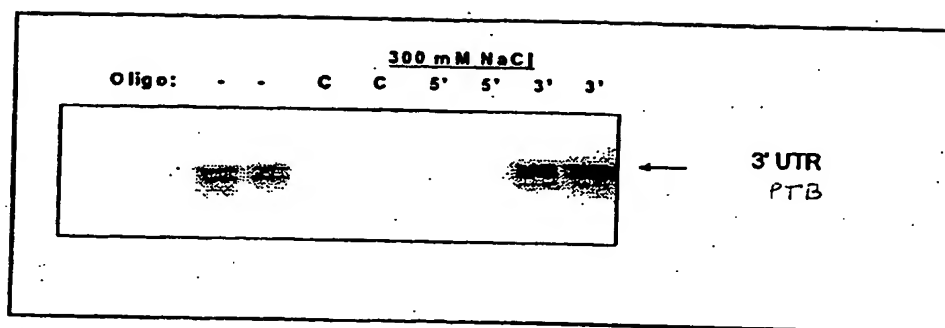
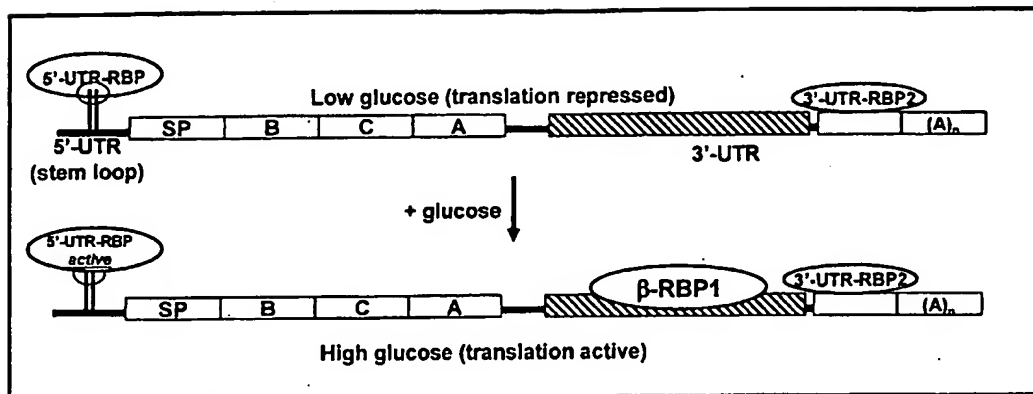


Figure 7



Model for binding of RBPs to preproinsulin mRNA

Figure 8

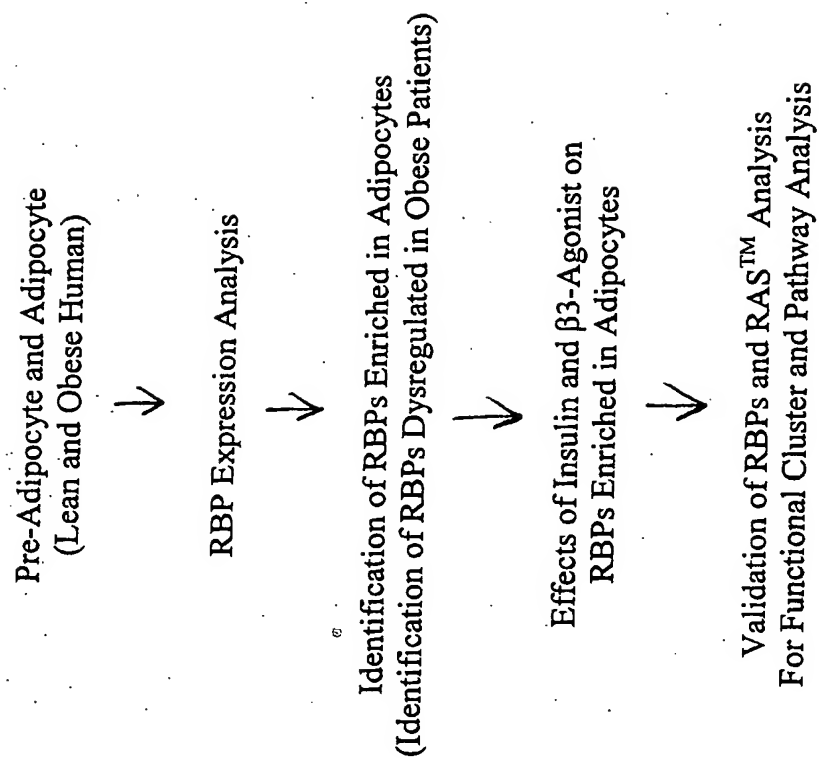


Figure 9

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank | | Description |
|--|--|---|-----------|--|
| | | Accession Number or Manufacturer Sequence | Reference | |
| NM_006413 | RPP30 | NP_006404 | | Homo sapiens ribonuclease P/RPP30 subunit (RPP30), mRNA |
| NM_020967 | NCOA5 | NP_066018 | | Homo sapiens nuclear receptor coactivator 5 (NCOA5), mRNA |
| NM_005058 | RBMY1A1 | NP_005049 | | Homo sapiens RNA binding motif protein, Y-linked, family 1, member A1 (RBMY1A1), mRNA |
| NM_018380 | DDX28 | NP_060850 | | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 28 (DDX28), nuclear gene encoding mitochondrial protein, mRNA |
| NM_020158 | RRP46 | NP_064543 | | Homo sapiens exosome component Rrp46 (RRP46), mRNA |
| XM_062047 | LOC120470 | XP_062047 | | Homo sapiens similar to discs, large (Drosophila) homolog 2; chapsyn-110 (LOC120470), mRNA |
| NM_003429 | ZNF85 | NP_003420 | | Homo sapiens zinc finger protein 85 (HPF4, HTF1) (ZNF85), mRNA |
| NM_005437 | NCOA4 | NP_005428 | | Homo sapiens nuclear receptor coactivator 4 (NCOA4), mRNA |
| NM_000281 | PCBD | NP_000272 | | Homo sapiens 6-pyruvoyl-tetrahydropterin synthase/dimerization cofactor of hepatocyte nuclear factor 1 alpha (TCF1) (PCBD), mRNA |
| NM_022915 | MRPL44 | NP_075066 | | Homo sapiens mitochondrial ribosomal protein L44 (MRPL44), nuclear gene encoding mitochondrial protein, mRNA |
| XM_068863 | LOC134477 | XP_068863 | | Homo sapiens similar to Hypothetical protein CGI-79 (LOC134477), mRNA |
| AK000256 | | BAA91036 | | Homo sapiens cDNA FLJ20249 fis, clone COLF6621 |
| NM_002197 | ACO1 | NP_002188 | | Homo sapiens aconitase 1, soluble (ACO1), mRNA |
| XM_066446 | LOC139051 | XP_066446 | | Homo sapiens similar to pol protein (LOC139051), mRNA |
| NM_000989 | RPL30 | NP_000980 | | Homo sapiens ribosomal protein L30 (RPL30), mRNA |
| NM_005119 | THRAP3 | NP_005110 | | Homo sapiens thyroid hormone receptor associated protein 3 (THRAP3), mRNA |
| AF254411 | SR-A1 | AAF87552 | | Homo sapiens serfarg-rich pre-mRNA splicing factor SR-A1 (SR-A1) gene, complete cds. |
| NM_006311 | NCOR1 | NP_006302 | | Homo sapiens nuclear receptor co-repressor 1 (NCOR1), mRNA |
| M58511 | IRE-BP2/IRP2 | AA669901 | | Human iron-responsive element-binding protein/iron regulatory protein 2 (IRE-BP2/IRP2) mRNA, partial cds. |

FIGURE 10

11/89

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | Description |
|--|--|---|---|
| XM_065361 | LOC129715 | XP_065361 | Homo sapiens similar to tudor protein (LOC129715), mRNA. |
| NM_019038 | TDRD4 | NP_061911 | Homo sapiens tudor domain containing 4 (TDRD4), mRNA. |
| NM_022768 | RBM15 | NP_073605 | Homo sapiens RNA binding motif protein 15 (RBM15), mRNA. |
| NM_000077 | CDKN2A | NP_000068 | Homo sapiens cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4) (CDKN2A), transcript variant 1, mRNA. |
| AB011167 | KIAA0595 | BAA25521 | Homo sapiens mRNA for KIAA0595 protein, partial cds. |
| NM_022360 | FAM12B | NP_071755 | Homo sapiens family with sequence similarity 12, member B (epididymal) (FAM12B), mRNA. |
| XM_091042 | LOC161682 | XP_091042 | Homo sapiens similar to data source:MGD, source key:MG1:107795, evidence:ISS-heterogeneous nuclear ribonucleoprotein C-putative (LOC161682), mRNA. |
| XM_089062 | LOC148866 | XP_089062 | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 (HELIX-DESTABILIZING PROTEIN) (SINGLE-STRAND BINDING PROTEIN) (HNRNP CORE PROTEIN A1) (LOC148866), mRNA. |
| XM_063247 | LOC122648 | XP_063247 | Homo sapiens similar to putative pancreatic ribonuclease (LOC122648), mRNA. |
| XM_061549 | LOC119579 | XP_061549 | Homo sapiens LOC119579 (LOC119579), mRNA. |
| NM_016200 | LSM8 | NP_057284 | Homo sapiens LSM8 homolog, U6 small nuclear RNA associated (S. cerevisiae) (LSM8), mRNA. |
| NM_017993 | FLJ10094 | NP_060463 | Homo sapiens hypothetical protein FLJ10094 (FLJ10094), mRNA. |
| XM_061319 | LOC119177 | XP_061319 | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 (HELIX-DESTABILIZING PROTEIN) (SINGLE-STRAND BINDING PROTEIN) (HNRNP CORE PROTEIN A1) (LOC119177), mRNA. |
| NM_007372 | DDX42 | NP_031398 | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 42 (DDX42), transcript variant 1, mRNA. |
| XM_092489 | LOC165271 | XP_092489 | Homo sapiens similar to heterogeneous nuclear ribonucleoprotein K (LOC165271), mRNA. |
| NM_000967 | RPL3 | NP_000958 | Homo sapiens ribosomal protein L3 (RPL3), mRNA. |
| NM_033117 | RBM18 | NP_149108 | Homo sapiens RNA binding motif protein 18 (RBM18), mRNA. |
| AF285599 | STK31 | AAK31978 | Homo sapiens serine/threonine kinase 31 (STK31) mRNA, complete cds. |
| NM_007363 | NONO | NP_031389 | Homo sapiens non-POU domain containing, octamer-binding (NONO), mRNA. |
| NM_002939 | RNH | NP_002930 | Homo sapiens ribonuclease/angiogenin inhibitor (RNH), transcript variant 1, mRNA. |

Figure 10

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank | | Description |
|--|--|---|--|-------------|
| | | Accession Number or Manufacturer Sequence | Reference | |
| XM_066901 | LOC139801 | XP_066901 | Homo sapiens LOC139801 (LOC139801), mRNA. | |
| NM_006074 | TRIM22 | NP_006065 | Homo sapiens tripartite motif-containing 22 (TRIM22), mRNA. | |
| XM_070605 | LOC137786 | XP_070605 | Homo sapiens similar to ANTIGEN GOR (LOC137786), mRNA. | |
| XM_090917 | LOC161461 | XP_090917 | Homo sapiens LOC161461 (LOC161461), mRNA. | |
| XM_093219 | LOC170270 | XP_093219 | Homo sapiens similar to Heterogeneous nuclear ribonucleoprotein A3 homolog 2 (hnRNP A3(B)) (LOC170270), mRNA. | |
| NM_004294 | MTRF1 | NP_004285 | Homo sapiens mitochondrial translational release factor 1 (MTRF1), nuclear gene encoding mitochondrial protein, mRNA | |
| NM_001605 | AARS | NP_001596 | Homo sapiens alanyl-tRNA synthetase (AARS), mRNA. | |
| XM_068154 | LOC133037 | XP_068154 | Homo sapiens LOC133037 (LOC133037), mRNA. | |
| XM_094140 | LOC166863 | XP_094140 | Homo sapiens similar to Apobec-1 complementation factor, APOBEC-1 stimulating protein (LOC166863), mRNA. | |
| X99302 | pop1 | CAA67684 | H.sapiens mRNA for Pop1 protein. | |
| XM_066606 | LOC139272 | XP_066606 | Homo sapiens similar to eukaryotic initiation factor 4B (LOC139272), mRNA. | |

Figure 10

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | | Description |
|--|--|---|--|--|
| | | | | |
| XM_070830 | LOC138280 | XP_070830 | | Homo sapiens similar to KIAA1138 protein (LOC138280), mRNA. |
| XM_092489 | LOC165271 | XP_092489 | | Homo sapiens similar to heterogeneous nuclear ribonucleoprotein K (LOC165271), mRNA. |
| NM_006413 | RPP30 | NP_006404 | | Homo sapiens ribonuclease P/MRP 30kDa subunit (RPP30), mRNA. |
| NM_002934 | RNASE2 | NP_002925 | | Homo sapiens ribonuclease, RNase A family, 2 (liver, eosinophil-derived neurotoxin) (RNASE2), mRNA. |
| NM_005058 | RBMV1A1 | NP_005049 | | Homo sapiens RNA binding motif protein, Y-linked, family 1, member A1 (RBMV1A1), mRNA. |
| NM_022360 | FAM12B | NP_071755 | | Homo sapiens family with sequence similarity 12, member B (epididymal) (FAM12B), mRNA. |
| XM_065361 | LOC129715 | XP_065361 | | Homo sapiens similar to tudor protein (LOC129715), mRNA. |
| NM_020967 | NCOA5 | NP_066018 | | Homo sapiens nuclear receptor coactivator 5 (NCOA5), mRNA. |
| NM_001024 | RPS21 | NP_001015 | | Homo sapiens ribosomal protein S21 (RPS21), mRNA. |
| NM_006187 | OAS3 | NP_006178 | | Homo sapiens 2'-5'-oligoadenylate synthetase 3, 100kDa (OAS3), mRNA. |
| NM_031994 | RNF17 | NP_114383 | | Homo sapiens ring finger protein 17 (RNF17), transcript variant short, mRNA. |
| XM_060358 | LOC127164 | XP_060358 | | Homo sapiens similar to TAR DNA binding protein (LOC127164), mRNA. |
| NM_002534 | OAS1 | NP_002525 | | Homo sapiens 2'-5'-oligoadenylate synthetase 1, 40/46kDa (OAS1), transcript variant E16, mRNA. |
| NM_018380 | DDX28 | NP_060850 | | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 28 (DDX28), nuclear gene encoding mitochondrial protein, mRNA. |

Figure 11

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | |
|--|--|---|--|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | Description |
| NM_025134 | FLJ12178 | NP_079410 | Homo sapiens hypothetical protein FLJ12178 (FLJ12178), mRNA. |
| XM_065361 | LOC129715 | XP_065361 | Homo sapiens similar to tudor protein (LOC129715), mRNA. |
| NM_004768 | SFRS11 | NP_004759 | Homo sapiens splicing factor, arginine/serine-rich 11 (SFRS11), mRNA. |
| XM_066446 | LOC139051 | XP_066446 | Homo sapiens similar to pol protein (LOC139051), mRNA. |
| NM_004592 | SFRS8 | NP_004583 | Homo sapiens splicing factor, arginine/serine-rich 8 (suppressor-of-white-apricot homolog, Drosophila) (SFRS8), transcript variant 2A, mRNA. |
| XM_069688 | LOC136068 | XP_069688 | Homo sapiens LOC136068 (LOC136068), mRNA. |
| NM_022830 | FLJ22347 | NP_073741 | Homo sapiens hypothetical protein FLJ22347 (FLJ22347), mRNA. |
| NM_013235 | RNASE3L | NP_037367 | Homo sapiens nuclear RNase III Drosha (RNASE3L), mRNA. |
| NM_003758 | EIF3S1 | NP_003749 | Homo sapiens eukaryotic translation initiation factor 3, subunit 1 alpha, 35kDa (EIF3S1), mRNA. |
| NM_005381 | NCL | NP_005372 | Homo sapiens nucleolin (NCL), mRNA. |
| NM_001145 | ANG | NP_001136 | Homo sapiens angiogenin, ribonuclease, RNase A family, 5 (ANG), mRNA. |
| XM_067085 | LOC140121 | XP_067085 | Homo sapiens similar to Heterogeneous nuclear ribonucleoprotein G (hnRNP G) (RNA binding motif protein, X chromosome) (LOC140121), mRNA. |
| XM_012988 | LOC151921 | XP_012968 | Homo sapiens similar to chromosome 20 open reading frame 14; putative mitochondrial outer membrane protein import receptor; similar to yeast pre-mRNA splicing factors, Prp1/Zer and Prp8 (LOC151921), mRNA. |
| NM_008170 | NOL1 | NP_006161 | Homo sapiens nucleolar protein 1, 120kDa (NOL1), mRNA. |
| NM_005617 | RPS14 | NP_005608 | Homo sapiens ribosomal protein S14 (RPS14), mRNA. |

Figure 12

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | | | Description |
|--|--|---|---|---|---|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | |
| NM_006546 | IMP-1 | NP_006537 | | | Homo sapiens IGF-II mRNA-binding protein 1 (IMP-1), mRNA. |
| NM_004689 | MTA1 | NP_004680 | | | Homo sapiens metastasis associated 1 (MTA1), mRNA. |
| NM_020143 | LOC56902 | NP_064528 | | | Homo sapiens putative 28 kDa protein (LOC56902), mRNA. |
| NM_003096 | SNRPG | NP_003087 | | | Homo sapiens small nuclear ribonucleoprotein polypeptide G (SNRPG), mRNA. |
| NM_000947 | PRIM2A | NP_000938 | | | Homo sapiens primase, polypeptide 2A, 58kDa (PRIM2A), mRNA. |
| NM_006312 | NCOR2 | NP_006303 | | | Homo sapiens nuclear receptor co-repressor 2 (NCOR2), mRNA. |

Figure 12

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | | | Description |
|--|--|---|---|---|--|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | |
| NM_006312 | NCOR2 | NP_006303 | | | Homo sapiens nuclear receptor co-repressor 2 (NCOR2), mRNA. |
| NM_006546 | IMP-1 | NP_006537 | | | Homo sapiens IGF-II mRNA-binding protein 1 (IMP-1), mRNA. |
| NM_020143 | LOC56902 | NP_064528 | | | Homo sapiens putative 28 kDa protein (LOC56902), mRNA. |
| XM_047499 | LOC149603 | XP_047499 | | | Homo sapiens hypothetical protein LOC149603 (LOC149603), mRNA. |
| NM_018415 | TRERF1 | NP_060885 | | | Homo sapiens transcriptional regulating factor 1 (TRERF1), transcript variant 3, mRNA. |
| NM_000947 | PRIM2A | NP_000938 | | | Homo sapiens primase, polypeptide 2A, 58kDa (PRIM2A), mRNA. |
| NM_013264 | DDX25 | NP_037396 | | | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 25 (DDX25), mRNA. |
| XM_095071 | CAGE | XP_095071 | | | Homo sapiens cancer-associated gene (CAGE), mRNA. |
| U23028 | | AAC50646 | | | Human eukaryotic initiation factor 2B-epsilon mRNA, partial cds. |
| NM_015891 | CDC40 | NP_056975 | | | Homo sapiens cell division cycle 40 homolog (yeast) (CDC40), mRNA. |
| NM_015453 | DKFZP434F091 | NP_056268 | | | Homo sapiens DKFZP434F091 protein (DKFZP434F091), mRNA. |
| NM_030794 | TDRD3 | NP_110421 | | | Homo sapiens tudor domain containing 3 (TDRD3), mRNA. |
| AF049523 | HYP A | AAC27501 | | | Homo sapiens huntingtin-interacting protein HYP A/FBP11 (HYP A), partial cds. |
| XM_088868 | LOC163412 | XP_088868 | | | Homo sapiens LOC163412 (LOC163412), mRNA. |
| NM_033030 | BOLL | NP_149019 | | | Homo sapiens bol, boule-like (Drosophila) (BOLL), transcript variant 2, mRNA. |
| NM_022915 | MRPL44 | NP_075066 | | | Homo sapiens mitochondrial ribosomal protein L44 (MRPL44), nuclear gene encoding mitochondrial protein mRNA. |
| XM_087251 | FLJ00166 | XP_087251 | | | Homo sapiens FLJ00166 protein (FLJ00166), mRNA. |
| NM_003096 | SNRPG | NP_003087 | | | Homo sapiens small nuclear ribonucleoprotein polypeptide G (SNRPG), mRNA. |
| NM_004937 | CTNS | NP_004928 | | | Homo sapiens cystinosis, nephropathic (CTNS), mRNA. |
| NM_004689 | MTA1 | NP_004680 | | | Homo sapiens metastasis associated 1 (MTA1), mRNA. |
| AF026126 | HNRPD | AAC23476 | | | Homo sapiens heterogeneous nuclear ribonucleoprotein D (HNRPD) gene, complete cds. |
| NM_002502 | NFKB2 | NP_002493 | | | Homo sapiens nuclear factor of kappa light polypeptide gene enhancer in B-cells 2 (p49/p100) (NFKB2), mRNA. |
| AF254411 | SR-A1 | AAF87552 | | | Homo sapiens ser/arg-rich pre-mRNA splicing factor SR-A1 (SR-A1) gene, complete cds. |

Figure 13

| Nucleotide | | | Protein Product | | |
|--------------|--------------|--------------------|--------------------|--|----|
| GenBank | GeneBank | | GeneBank | | |
| Accession | Accesssion | | Accesssion | | |
| Number or | Number or | | Number or | | |
| Manufacturer | Manufacturer | | Manufacturer | | |
| Sequence ID | Probe Name | Sequence Reference | Sequence Reference | | |
| XM_064989 | LOC126205 | XP_064989 | | Homo sapiens similar to PYRIN-containing APAF1-like protein 7; PYRIN-containing APAF1-like protein mRNA; monarch 1 [Homo sapiens] (LOC126205), mRNA. | 0 |
| XM_070263 | LOC137165 | XP_070263 | | Homo sapiens similar to ribosomal protein L3; 60S ribosomal protein L3; HIV-1 TAR RNA-binding protein B (LOC137165), mRNA. | 00 |
| NM_006388 | HTATIP | NP_006379 | | Homo sapiens HIV-1 Tat interactive protein, 60kDa (HTATIP), transcript variant 2, mRNA. | 01 |
| NM_006209 | ENPP2 | NP_006200 | | Homo sapiens ectonucleotide pyrophosphatase/phosphodiesterase 2 (autotaxin) (ENPP2), mRNA. | |
| BC012090 | | AAH12090 | | Homo sapiens, Similar to heterogeneous nuclear ribonucleoprotein A3, clone MGC:20045 IMAGE:4661041 mRNA, complete cds. | |
| NM_001019 | RPS15A | NP_001010 | | Homo sapiens ribosomal protein S15a (RPS15A), mRNA. | |
| NM_021133 | RNASEL | NP_066956 | | Homo sapiens ribonuclease L (2',5'-oligoadenylate synthetase-dependent) (RNASEL), mRNA. | |
| NM_013235 | RNASE3L | NP_037367 | | Homo sapiens nuclear RNase III Drosha (RNASE3L), mRNA. | |
| NM_015235 | CSTF2T | NP_056050 | | Homo sapiens cleavage stimulation factor, 3' pre-RNA, subunit 2, 64kDa, tau variant (CSTF2T), mRNA. | |
| NM_004094 | EIF2S1 | NP_004085 | | Homo sapiens eukaryotic translation initiation factor 2, subunit 1 alpha, 35kDa (EIF2S1), mRNA. | |
| NM_006163 | NFE2 | NP_006154 | | Homo sapiens nuclear factor (erythroid-derived 2), 45kDa (NFE2), mRNA. | |
| NM_014003 | DHX38 | NP_054722 | | Homo sapiens nuclear factor (erythroid-derived 2), 45kDa (NFE2), mRNA. | |
| NM_006789 | APOBEC2 | NP_006780 | | Homo sapiens DEAH (Asp-Glu-Ala-His) box polypeptide 38 (DHX38), mRNA. | |
| NM_014285 | RRP4 | NP_055100 | | Homo sapiens apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 2 (APOBEC2), mRNA. | |
| | | | | Homo sapiens homolog of Yeast RRP4 (ribosomal RNA processing 4), 3'-5'-exoribonuclease (RRP4), mRNA. | |
| NM_004175 | SNRPD3 | NP_004166 | | Homo sapiens small nuclear ribonucleoprotein D3 polypeptide 18kDa (SNRPD3), mRNA. | |
| AL117473 | DKFZp727A071 | CAB55948 | | Homo sapiens mRNA; cDNA DKFZp727A071 (from clone DKFZp727A071); partial cds. | |
| XM_085059 | LOC145223 | XP_085059 | | Homo sapiens similar to Splicing factor 3B subunit 4 (Spliceosome associated protein 49) (SAP 49) (SF3b5 (Pre-mRNA splicing factor SF3b 49 kDa subunit) (LOC145223), mRNA. | |

Figure 13

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | | | Description |
|--|--|---|---|---|---|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | |
| NM_020158 | RRP46 | NP_064543 | | | Homo sapiens exosome component Rrp46 (RRP46), mRNA. |
| NM_016024 | CGI-79 | NP_057108 | | | Homo sapiens CGI-79 protein (CGI-79), mRNA. |
| XM_065361 | LOC129715 | XP_065361 | | | Homo sapiens similar to tudor protein (LOC129715), mRNA. |
| XM_068863 | LOC134477 | XP_068863 | | | Homo sapiens similar to Hypothetical protein CGI-79 (LOC134477), mRNA. |
| NM_006527 | SLBP | NP_006518 | | | Homo sapiens stem-loop (histone) binding protein (SLBP), mRNA. |
| NM_024321 | MGC10433 | NP_077297 | | | Homo sapiens hypothetical protein MGC10433 (MGC10433), mRNA. |
| NM_003075 | SMARCC2 | NP_003066 | | | Homo sapiens SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 2 (SMARCC2), transcript variant 1, mRNA. |
| NM_016955 | SLALP | NP_058651 | | | Homo sapiens soluble liver antigen/liver pancreas antigen (SLALP), mRNA. |
| NM_002819 | PTBP1 | NP_002810 | | | Homo sapiens polypyrimidine tract binding protein 1 (PTBP1), transcript variant 1, mRNA. |
| NM_001021 | RPS17 | NP_001012 | | | Homo sapiens ribosomal protein S17 (RPS17), mRNA. |
| NM_002568 | PABPC1 | NP_002559 | | | Homo sapiens poly(A) binding protein, cytoplasmic 1 (PABPC1), mRNA. |
| NM_014871 | USP52 | NP_055686 | | | Homo sapiens ubiquitin specific protease 52 (USP52), mRNA. |
| NM_003076 | SMARCD1 | NP_003067 | | | Homo sapiens SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 1 (SMARCD1), transcript variant 1, mRNA. |
| NM_006547 | IMP-3 | NP_006538 | | | Homo sapiens IGF-II mRNA-binding protein 3 (IMP-3), mRNA. |
| NM_025134 | FLJ12178 | NP_079410 | | | Homo sapiens hypothetical protein FLJ12178 (FLJ12178), mRNA. |
| NM_002695 | POLR2E | NP_002686 | | | Homo sapiens polymerase (RNA) II (DNA directed) polypeptide E, 25kDa (POLR2E), mRNA. |
| NM_005801 | SUI1 | NP_005792 | | | Homo sapiens putative translation initiation factor (SUI1), mRNA. |
| NM_022830 | FLJ22347 | NP_073741 | | | Homo sapiens hypothetical protein FLJ22347 (FLJ22347), mRNA. |
| NM_012245 | SNW1 | NP_036377 | | | Homo sapiens SKI-interacting protein (SNW1), mRNA. |
| NM_005617 | RPS14 | NP_005608 | | | Homo sapiens ribosomal protein S14 (RPS14), mRNA. |
| NM_021134 | MRPL23 | NP_066957 | | | Homo sapiens mitochondrial ribosomal protein L23 (MRPL23), nuclear gene encoding mitochondrial protein mRNA. |

Figure 13

| | | | |
|-----------|-----------|-----------|--|
| XM_058421 | LOC119832 | XP_058421 | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 (HELIX- DESTABILIZING PROTEIN) (SINGLE-STRAND BINDING PROTEIN) (HNRNP CORE PROTEIN A1) (LOC119832), mRNA. |
| NM_006013 | RPL10 | NP_006004 | Homo sapiens ribosomal protein L10 (RPL10), mRNA. |

Figure 13

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | |
|---|---|---|--|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | Description |
| XM_085111 | LOC145359 | | Homo sapiens similar to RIBONUCLEASE PANCREATIC PRECURSOR (RNASE A) (LOC145359), mRNA |
| XM_047920 | LOC92906 | | Homo sapiens similar to Unknown (protein for IMAGE:3587716) (LOC92906), mRNA |
| XM_060628 | LOC127722 | | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 (HELIX-DESTABILIZING PROTEIN) (SINGLE-STRAND BINDING PROTEIN) (HNRNP CORE PROTEIN A1) (UNWINDING PROTEIN 1) (UP1) (LOC127722), mRNA |
| XM_088640 | LOC158685 | | Homo sapiens similar to RNA-binding region (RNP1, RRM) containing 2 (H. sapiens) (LOC158685), mRNA |
| XM_017931 | LOC158201 | | Homo sapiens similar to RNA binding motif protein, X chromosome (H. sapiens) (LOC158201), mRNA |
| XM_062047 | LOC120470 | | Homo sapiens similar to discs, large (Drosophila) homolog 2; chapsyn-110 (LOC120470), mRNA |
| XM_068997 | LOC134759 | | Homo sapiens similar to heterogeneous nuclear ribonucleoprotein L (LOC134759), mRNA |
| XM_087697 | LOC153522 | | Homo sapiens similar to splicing factor, arginine/serine-rich 11 (LOC153522), mRNA |
| NM_003191 | TARS | | Homo sapiens threonyl-tRNA synthetase (TARS), mRNA |
| XM_061850 | LOC120083 | | Homo sapiens similar to 46KD arginine/serine-rich splicing factor (LOC120083), mRNA |
| XM_093219 | LOC170270 | | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A3 HOMOLOG 2 (HNRNP A3(B)) (LOC170270), mRNA |
| XM_068457 | LOC133655 | | Homo sapiens similar to splicing coactivator subunit SRm300; RNA binding protein; AT-rich element binding factor; serine/arginine repetitive matrix 2 (LOC133655), mRNA |
| NM_014892 | KIAA1116 | | Homo sapiens KIAA1116 protein (KIAA1116), mRNA |
| XM_058819 | LOC124540 | | Homo sapiens similar to RNA-binding protein Musashi2-S (LOC124540), mRNA |
| XM_058653 | LOC122651 | | Homo sapiens similar to RIBONUCLEASE PANCREATIC (RNASE A) (LOC122651), mRNA |
| XM_093626 | LOC152108 | | Homo sapiens similar to ubiquitin A-52 residue ribosomal protein fusion product 1 (LOC152108), mRNA |
| XM_061002 | LOC118523 | | Homo sapiens similar to SON DNA binding protein; SON DNA-binding protein; SON DNA-binding protein, KIAA1019; NRE-binding protein (H. sapiens) (LOC118523), mRNA |
| XM_060358 | LOC127164 | | Homo sapiens similar to TAR DNA binding protein (LOC127164), mRNA |

Figure 14

| Nucleotide | | Protein Product | | Description |
|--|-------------------------|--------------------------------------|--|--|
| GenBank Accession Number or Manufacturer Sequence ID | Manufacturer Probe Name | Gene Name or Manufacturer Probe Name | GeneBank Accession Number or Manufacturer Sequence Reference | |
| XM_063601 | | LOC123341 | | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 (HELIX-DESTABILIZING PROTEIN) (SINGLE-STRAND BINDING PROTEIN) (HNRNP CORE PROTEIN A1) (UNWINDING PROTEIN 1) (UPI1) (LOC123341), mRNA. |
| XM_059612 | | LOC132928 | | Homo sapiens similar to poly(A) binding protein, cytoplasmic 1; poly(A)-binding protein, cytoplasmic 1 (LOC132928), mRNA. |
| NM_021993 | | FUSIP1 | | Homo sapiens FUS interacting protein (serine-arginine rich) 1 (FUSIP1) transcript variant 2, mRNA. |
| XM_064113 | | LOC124380 | | Homo sapiens similar to Hrb27C-P1; RNA-binding protein 7 (LOC124380), mRNA. |
| XM_098297 | | LOC153028 | | Homo sapiens similar to RNA binding protein S1, serine-rich domain (H. sapiens) (LOC153028), mRNA. |
| XM_062934 | | LOC122056 | | Homo sapiens similar to ATP-DEPENDENT RNA HELICASE A (NUCLEAR DNA HELICASE II) (NDH II) (DEAD-BOX PROTEIN 5) (LOC122056), mRNA. |
| XM_053153 | | LOC149973 | | Homo sapiens similar to RNA binding motif protein, X chromosome (H. sapiens) (LOC149973), mRNA. |
| XM_070603 | | LOC137784 | | Homo sapiens similar to ANTIGEN GOR (LOC137784), mRNA. |
| XM_086419 | | LOC149092 | | Homo sapiens similar to pumilio homolog 1 (Drosophila) (H. sapiens) (LOC149092), mRNA. |
| XM_067918 | | LOC132583 | | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 (HELIX-DESTABILIZING PROTEIN) (SINGLE-STRAND BINDING PROTEIN) (HNRNP CORE PROTEIN A1) (LOC132583), mRNA. |
| NM_008450 | | SPF45 | | Homo sapiens splicing factor (45kD) (SPF45), mRNA. |
| NM_004940 | | DDX7 | | Homo sapiens DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 7 (RNA helicase, 52kD) (DDX7), mRNA. |
| XM_086011 | | LOC148027 | | Homo sapiens similar to bruno-like 5, RNA binding protein (Drosophila); Bruno (Drosophila) -like 5, RNA binding protein CUG-BP and ETR-3 like factor 5; RNA-binding protein BRUNOL-5 (LOC148027), mRNA. |
| XM_073386 | | LOC119594 | | Homo sapiens similar to SPLICING FACTOR U2AF 65 KDA SUBUNIT (U2AF65) (LOC119594), mRNA. |
| XM_067051 | | LOC140065 | | SNRNP AUXILIARY FACTOR LARGE SUBUNIT (U2AF65) (LOC140065), mRNA. |
| NM_003138 | | SRPK2 | | Homo sapiens similar to RNA binding motif protein, Y chromosome, family 1, member A1; RNA binding motif protein 1; RNA binding motif protein 2 (LOC140065), mRNA. |
| XM_092386 | | LOC165115 | | Homo sapiens SFRS protein kinase 2 (SRPK2), mRNA. |
| | | | | Homo sapiens similar to KIAA1841 protein (LOC165115), mRNA. |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | |
|---|---|---|---|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | Description |
| XM_062047 | LOC120470 | | Homo sapiens similar to discs, large (Drosophila) homolog 2; chapsyn-110 (LOC120470), mRNA. |
| XM_092031 | LOC163147 | | Homo sapiens similar to splicing factor 3a, subunit 2, 66kD; Spliceosome protein SAP-62 (LOC163147), mRNA. |
| XM_067074 | LOC140100 | | Homo sapiens similar to RNA binding motif protein, Y chromosome, family 1, member A1; RNA binding motif protein 1; RNA binding motif protein 2 (LOC140100), mRNA. |
| XM_060102 | LOC126635 | | Homo sapiens similar to splicing factor, arginine/serine-rich 2, interacting protein; SC35-Interacting protein 1 (LOC126635), mRNA. |
| XM_001524 | LOC151173 | | Homo sapiens similar to TAR DNA binding protein (H. sapiens) (LOC151173), mRNA. |
| XM_086782 | LOC150152 | | Homo sapiens similar to SPLICING FACTOR U2AF 35 KD SUBUNIT (U2 AUXILIARY FACTOR 35 KD SUBUNIT) (U2 SNRNP AUXILIARY FACTOR SMALL SUBUNIT) (LOC150152), mRNA. |
| XM_070605 | LOC137786 | | Homo sapiens similar to ANTIGEN GOR (LOC137786), mRNA. |
| NM_008842 | SF3B2 | | Homo sapiens splicing factor 3b, subunit 2, 145kD (SF3B2), mRNA. |
| XM_095899 | LOC169732 | | Homo sapiens similar to EXOSOME COMPLEX EXONUCLEASE RRP4 (RIBOSOMAL RNA PROCESSING PROTEIN 4) (LOC169732), mRNA. |
| XM_066446 | LOC139051 | | Homo sapiens similar to hypothetical protein (LOC139051), mRNA. |
| XM_089765 | LOC143344 | | Homo sapiens similar to poly(A) binding protein (LOC143344), mRNA. |
| XM_089587 | LOC159428 | | Homo sapiens similar to EUKARYOTIC TRANSLATION INITIATION FACTOR 4B (EIF-4B) (LOC159428), mRNA. |
| XM_092043 | LOC163160 | | Homo sapiens similar to polypyrimidine tract binding protein, isoform b; heterogeneous nuclear ribonucleoprotein polypeptide b; RNA binding protein (LOC163160), mRNA. |
| XM_091270 | LOC161983 | | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 (HELIX-DESTABILIZING PROTEIN) (SINGLE-STRAND BINDING PROTEIN) (HNRNP CORE PROTEIN A1) (LOC161983), mRNA. |
| XM_067072 | LOC140098 | | Homo sapiens similar to RBM1 (LOC140098), mRNA. |
| XM_056568 | LOC147774 | | Homo sapiens similar to KH-type splicing regulatory protein (FUSE binding protein 2) (H. sapiens) (LOC147774), mRNA. |

Figure 14

| Nucleotide | | Protein Product | |
|--|-------------------------|---|--|
| GenBank Accession Number or Manufacturer Sequence ID | Manufacturer Probe Name | Gene Name or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference |
| XM_091235 | LOC161931 | Homo sapiens similar to hypothetical protein (LOC161931), mRNA | |
| XM_058943 | LOC125925 | Homo sapiens similar to R32611_1 (LOC125925), mRNA | |
| XM_058876 | LOC124944 | Homo sapiens similar to putative (H. sapiens) (LOC124944), mRNA | |
| XM_088975 | LOC148683 | Homo sapiens similar to pumilio homolog 1 (Drosophila); pumilio (Drosophila) homolog 1 (LOC148683), mRNA | |
| XM_092221 | LOC164891 | Homo sapiens similar to mRNA for ribosomal protein S9 (LOC164891), mRNA | |
| XM_095591 | LOC169242 | Homo sapiens similar to putative (LOC169242), mRNA | |
| XM_093336 | LOC165631 | Homo sapiens similar to KIAA1268 protein (LOC165631), mRNA | |
| XM_065002 | LOC126246 | Homo sapiens similar to Similar to splicing factor proline/glutamine rich (polypyrimidine tract-binding protein-associated) (H. sapiens) (LOC126246), mRNA | |
| XM_067452 | LOC131596 | Homo sapiens similar to splicing factor 3a, subunit 2, 66kD; Spliceosome protein SAP-62 (LOC131596), mRNA | |
| XM_062601 | LOC121365 | Homo sapiens similar to RBM1 (LOC121365), mRNA | |
| XM_088248 | LOC133225 | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 (HELIX-DESTABILIZING PROTEIN) (SINGLE-STRAND BINDING PROTEIN) (HNRNP CORE PROTEIN A1) (H. sapiens) (LOC133225), mRNA | |
| XM_068022 | LOC132772 | Homo sapiens similar to split ends; polycyphalon; yippee interacting protein 1 (LOC132772), mRNA | |
| XM_066901 | LOC139801 | Homo sapiens similar to splicing factor, arginine/serine-rich 4 (SFRP75); similar to splicing factor, arginine/serine-rich 4 (SFRSA) (H. sapiens) (LOC139801), mRNA | |
| XM_067087 | LOC140123 | Homo sapiens similar to RNA binding protein (LOC140123), mRNA | |
| XM_067844 | LOC132430 | Homo sapiens similar to poly(A)-binding protein, cytoplasmic 4 (inducible form); inducible poly(A)-binding protein (LOC132430), mRNA | |
| XM_070624 | LOC137819 | Homo sapiens similar to Rbm (H. sapiens) (LOC137819), mRNA | |
| BC005054 | | Homo sapiens, clone IMAGE:2822202, mRNA, partial cds. | AAH05054 |
| NM_031994 | RNF17 | Homo sapiens ring finger protein 17 (RNF17), transcript variant short, mRNA | NP_114383 |

| Nucleotide | | Protein Product | | Description |
|-------------------|------------------------|---------------------------|---------------------------|--|
| GenBank Accession | Number or Manufacturer | Gene Name or Manufacturer | Gene Name or Manufacturer | |
| Sequence ID | Sequence | Probe Name | Reference | |
| HSU87589 | | | AAB63112 | Human endogenous retrovirus clone K1.1 polymerase mRNA, partial cds. |
| XM_085111 | | LOC145359 | XP_085111 | Homo sapiens similar to Ribonuclease pancreatic precursor (RNase A) (LOC145359), mRNA. |
| NM_024045 | | DDX50 | NP_076950 | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 50 (DDX50), mRNA. |
| NM_001021 | | RPS17 | NP_001012 | Homo sapiens ribosomal protein S17 (RPS17), mRNA. |
| AC004957 | | | | Homo sapiens PAC clone RP5-1093O17 from 7, complete sequence. |
| NM_004792 | | PPIG | NP_004783 | Homo sapiens peptidyl-prolyl isomerase G (cyclophilin G) (PPIG), mRNA. |
| NM_001011 | | RPS7 | NP_001002 | Homo sapiens ribosomal protein S7 (RPS7), mRNA. |
| XM_047920 | | LOC92906 | XP_047920 | Homo sapiens similar to Unknown (protein for IMAGE:3587716) (LOC92906), mRNA. |
| AI088192 | | | | oz97g12.x1 Soares_parathyroid_tumor_NbHPA Homo sapiens cDNA clone IMAGE:1683334 3' similar to TR:Q38800 Q388 COL-O PUTATIVE RNA HELICASE A.; mRNA sequence. |
| NM_005058 | | RBMY1A1 | NP_005049 | Homo sapiens RNA binding motif protein, Y-linked, family 1, member A1 (RBMY1A1), mRNA. |
| XM_060628 | | LOC127722 | XP_060628 | Homo sapiens similar to Heterogeneous nuclear ribonucleoprotein A1 (Helix-stabilizing protein) (Single-strand binding protein) (hnRNP core protein A1) (HDP-1) (Topoisomerase-inhibitor suppressed) (LOC127722), mRNA. |
| NM_020867 | | NCOA5 | NP_066018 | Homo sapiens nuclear receptor coactivator 5 (NCOA5), mRNA. |
| NM_006275 | | SFRS6 | NP_006266 | Homo sapiens splicing factor, arginine/serine-rich 6 (SFRS6), mRNA. |
| XM_088640 | | LOC158685 | XP_088640 | Homo sapiens similar to bA353C18.3.2 (splicing factor CC1.3, isoform 2 (CC1.4)) (LOC158685), mRNA. |
| XM_017931 | | LOC158201 | XP_017931 | Homo sapiens similar to Heterogeneous nuclear ribonucleoprotein G (hnRNP G) (Glycoprotein P43) (LOC158201), mRNA. |
| NM_005016 | | PCBP2 | NP_005007 | Homo sapiens poly(rC) binding protein 2 (PCBP2), transcript variant 1, mRNA. |
| NM_006713 | | PC4 | NP_006704 | Homo sapiens activated RNA polymerase II transcription cofactor 4 (PC4), mRNA. |
| NM_018427 | | RRN3 | NP_060897 | Homo sapiens RNA polymerase I transcription factor RRN3 (RRN3), mRNA. |
| NM_004960 | | FUS | NP_004951 | Homo sapiens fusion (Involved in t(12;16) in malignant liposarcoma) (FUS), mRNA. |
| AF267533 | | | AAF78955 | Homo sapiens CUG-binding protein LYQ isoform mRNA, complete cds. |
| XM_062047 | | LOC120470 | XP_062047 | Homo sapiens similar to discs, large (Drosophila) homolog 2; chapsyn-110 (LOC120470), mRNA. |

Figure 14

| Nucleotide | | Protein Product | |
|------------------------------------|---------------------------|---|--------------|
| GenBank Accession | Gene Name or Manufacturer | GeneBank Accession | Manufacturer |
| Number or Manufacturer Sequence ID | Manufacturer Probe Name | Number or Manufacturer Sequence Reference | Manufacturer |
| NM_003797 | EED | NP_003788 | |
| NM_001025 | RPS23 | NP_001016 | |
| NM_005156 | ROD1 | NP_005147 | |
| BC001050 | NFATC3 | AAH01050 | |
| NM_000281 | PCBD | NP_000272 | |
| XM_068997 | LOC134759 | XP_068997 | |
| NM_005887 | DLEU1 | NP_005878 | |
| AF435977 | SON | AAL30810 | |
| NM_001002 | RPLP0 | NP_000993 | |
| NM_000989 | RPL30 | NP_000980 | |
| XM_087697 | LOC153522 | XP_087697 | |
| AC004957 | | | |
| NM_004902 | RNPC2 | NP_004893 | |
| NM_003191 | TARS | NP_003182 | |
| NM_021177 | LSM2 | NP_067000 | |
| NM_002948 | RPL15 | NP_002939 | |
| XM_061850 | LOC120083 | XP_061850 | |
| NM_004705 | PRKRIR | NP_004696 | |
| XM_093219 | LOC170270 | XP_093219 | |
| HSP01 | pop1 | CAA67684 | |
| NM_001429 | EP300 | NP_001420 | |

Figure 14

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | | | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | | Description |
|---|-----------|-----------|---|--|-------------|
| Gene Name or Manufacturer Probe Name | | | | | |
| NM_014168 | HSPC133 | NP_054887 | Homo sapiens HSPC133 protein (HSPC133), mRNA. | | |
| NM_001968 | EIF4E | NP_001959 | Homo sapiens eukaryotic translation initiation factor 4E (EIF4E), mRNA. | | |
| NM_005968 | HNRPM | NP_005959 | Homo sapiens heterogeneous nuclear ribonucleoprotein M (HNRPM), transcript variant 1, mRNA. | | |
| NM_006372 | SYNCRIP | NP_006363 | Homo sapiens synaptotagmin binding, cytoplasmic RNA interacting protein (SYNCRIP), mRNA. | | |
| NM_002136 | HNRPA1 | NP_002127 | Homo sapiens heterogeneous nuclear ribonucleoprotein A1 (HNRPA1), transcript variant 1, mRNA. | | |
| NM_006638 | RPP40 | NP_006629 | Homo sapiens ribonuclease P 40kDa subunit (RPP40), mRNA. | | |
| NM_004539 | NARS | NP_004530 | Homo sapiens asparaginyl-tRNA synthetase (NARS), mRNA. | | |
| AC004957 | | | Homo sapiens PAC clone RP5-1093O17 from 7, complete sequence. | | |
| HS164F3 | dJ164F3.1 | CAB55879 | Human DNA sequence from clone RP1-164F3 on chromosome Xq21.33-23 Contains genes for DFN1 (deafness, X-linked 1 progressive, DDP (X-LINKED DEAFNESS DYSTONIA PROTEIN)), BTK(Bruton agammaglobulinemia tyrosine kinase), RPL44(L44-like ribosomal protein), GLA (galactosidase, alpha) and FTP3 (HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN), ESTs, STSs, GSSs and CpG Islands, complete sequence. | | |
| BC016283 | ABCE1 | AAH16283 | Homo sapiens ATP-binding cassette, sub-family E (OABP), member 1, mRNA (cDNA clone MGC:3909151), complete cds. | | |
| NM_006392 | NOL5A | NP_006383 | Homo sapiens nucleolar protein 5A (56kDa with KKEJD repeat) (NOL5A), mRNA. | | |
| BC002395 | SF3A3 | AAH02395 | Homo sapiens splicing factor 3a, subunit 3, 60kDa, mRNA (cDNA clone MGC:8445 IMAGE:2821350), complete cds. | | |
| NM_003769 | SFRS9 | NP_003760 | Homo sapiens splicing factor, arginine/serine-rich 9 (SFRS9), mRNA. | | |
| NM_006743 | RBM3 | NP_006734 | Homo sapiens RNA binding motif protein 3 (RBM3), mRNA. | | |
| AF165518 | MAGOH | AAF86648 | Homo sapiens MAGOH isoform (MAGOH) mRNA, complete cds. | | |
| NM_001402 | EEF1A1 | NP_001393 | Homo sapiens eukaryotic translation elongation factor 1 alpha 1 (EEF1A1), mRNA. | | |
| NM_030594 | CPEB1 | NP_085097 | Homo sapiens cytoplasmic polyadenylation element binding protein 1 (CPEB1), mRNA. | | |
| NM_001024 | RPS21 | NP_001015 | Homo sapiens ribosomal protein S21 (RPS21), mRNA. | | |

Figure 14

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | | Description | Variant |
|---|---|---|---------------------------------------|--|---------|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | Manufacturer Sequence Reference | | |
| NM_003488 | AKAP1 | NP_003479 | | Homo sapiens A kinase (PRKA) anchor protein 1 (AKAP1), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA. | 1 |
| AF038362 | TAF-172 | AAC04573 | | Homo sapiens TBP-associated factor 172 (TAF-172) mRNA, complete cds. | 2 |
| NM_004501 | HNRPU | NP_004492 | | Homo sapiens heterogeneous nuclear ribonucleoprotein U (scaffold attachment factor A) (HNRPU), transcript variant 2, mRNA. | 3 |
| NM_004396 | DDX5 | NP_004387 | | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 5 (DDX5), mRNA. | |
| NM_000968 | RPL4 | NP_000959 | | Homo sapiens ribosomal protein L4 (RPL4), mRNA. | |
| NM_001028 | RPS25 | NP_001019 | | Homo sapiens ribosomal protein S25 (RPS25), mRNA. | |
| NM_007367 | RALY | NP_031393 | | Homo sapiens RNA binding protein (autobalogenic, hnRNP-associated with lethal yellow) (RALY), transcript variant 2, mRNA. | |
| NM_004689 | MTA1 | NP_004680 | | Homo sapiens metastasis associated 1 (MTA1), mRNA. | |
| XM_068457 | LOC133655 | XP_068457 | | Homo sapiens similar to splicing coactivator subunit SRm300; RNA binding protein; AT-rich element binding factor; serine/arginine repetitive matrix 2 (LOC133655), mRNA. | |
| NM_003754 | EIF3S5 | NP_003745 | | Homo sapiens eukaryotic translation initiation factor 3, subunit 5 epsilon, 47kDa (EIF3S5), mRNA. | |
| AC004957 | | | | Homo sapiens PAC clone RP5-1093O17 from 7, complete sequence. | |
| AC004957 | | | | Homo sapiens PAC clone RP5-1093O17 from 7, complete sequence. | |
| NM_006711 | RNPS1 | NP_006702 | | Homo sapiens RNA binding protein S1, serine-rich domain (RNPS1), transcript variant 1, mRNA. | |
| NM_016480 | PAIP2 | NP_057564 | | Homo sapiens poly(A) binding protein interacting protein 2 (PAIP2), mRNA. | |
| NM_001014 | RPS10 | NP_001005 | | Homo sapiens ribosomal protein S10 (RPS10), mRNA. | |
| AF070668 | | AAC02074 | | Homo sapiens 40S ribosomal protein S27 isoform mRNA, complete cds. | |
| NM_006938 | SNRPD1 | NP_008869 | | Homo sapiens small nuclear ribonucleoprotein D1 polypeptide 16kDa (SNRPD1), mRNA. | |
| NM_014892 | RBM16 | NP_055707 | | Homo sapiens RNA binding motif protein 16 (RBM16), mRNA. | |
| NM_018353 | C14orf106 | NP_060823 | | Homo sapiens chromosome 14 open reading frame 106 (C14orf106), mRNA. | |
| NM_006196 | PCBP1 | NP_006187 | | Homo sapiens poly(C) binding protein 1 (PCBP1), mRNA. | |
| XM_058819 | MSI2 | XP_058819 | | Homo sapiens musashi homolog 2 (Drosophila) (MSI2), mRNA. | |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | |
|---|---|---|--|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | Description |
| NM_003133 | SRP9 | NP_003124 | Homo sapiens signal recognition particle 9kDa (SRP9), mRNA |
| NM_001016 | RPS12 | NP_001007 | Homo sapiens ribosomal protein S12 (RPS12), mRNA |
| NM_004516 | ILF3 | NP_004507 | Homo sapiens interleukin enhancer binding factor 3, 90kDa (ILF3), transcript variant 2, mRNA |
| XM_058653 | LOC122651 | XP_058653 | Homo sapiens LOC122651 (LOC122651), mRNA |
| NM_003750 | EIF3S10 | NP_003741 | Homo sapiens eukaryotic translation initiation factor 3, subunit 10 theta, 150/170kDa (EIF3S10), mRNA |
| AK054960 | | | Homo sapiens cDNA FLJ30398 fis, clone BRACE2008402, highly similar to Homo sapiens steroid receptor RNA activator isoform 3 mRNA |
| NM_017697 | FLJ20171 | NP_060167 | Homo sapiens hypothetical protein FLJ20171 (FLJ20171), mRNA |
| NM_000985 | RPL17 | NP_000976 | Homo sapiens ribosomal protein L17 (RPL17), mRNA |
| HSM801037 | | | Homo sapiens mRNA; cDNA DKFZp434L1935 (from clone DKFZp434L1935) |
| NM_014060 | MCTS1 | NP_054779 | Homo sapiens malignant T cell amplified sequence 1 (MCTS1), mRNA |
| NM_014463 | LSM3 | NP_055278 | Homo sapiens LSM3 homolog; U6 small nuclear RNA associated (S. cerevisiae) (LSM3), mRNA |
| AF294007 | | AAG31577 | Homo sapiens haplotype 1 eosinophil-derived neurotoxin gene, complete cds |
| NM_003092 | SNRPB2 | NP_003083 | Homo sapiens small nuclear ribonucleoprotein polypeptide B' (SNRPB2), transcript variant 1, mRNA |
| NM_001418 | EIF4G2 | NP_001409 | Homo sapiens eukaryotic translation initiation factor 4 gamma, 2 (EIF4G2), mRNA |
| NM_006802 | SF3A3 | NP_006793 | Homo sapiens splicing factor 3a, subunit 3, 60kDa (SF3A3), mRNA |
| XM_093626 | LOC152108 | XP_093626 | Homo sapiens similar to ubiquitin A-52 residue ribosomal protein fusion product 1 (LOC152108), mRNA |
| BC000138 | HNRPM | AAH00138 | Homo sapiens heterogeneous nuclear ribonucleoprotein M, transcript variant 1, mRNA (cDNA clone MGC:5136 IMAGE:2900532), complete cds |
| NM_007040 | HNRPUL1 | NP_008971 | Homo sapiens heterogeneous nuclear ribonucleoprotein U-like 1 (HNRPUL1), transcript variant 1, mRNA |
| NM_003908 | EIF2S2 | NP_003899 | Homo sapiens eukaryotic translation initiation factor 2, subunit 2 beta, 38kDa (EIF2S2), mRNA |
| NM_000994 | RPL32 | NP_000985 | Homo sapiens ribosomal protein L32 (RPL32), mRNA |
| NM_003757 | EIF3S2 | NP_003748 | Homo sapiens eukaryotic translation initiation factor 3, subunit 2 beta, 36kDa (EIF3S2), mRNA |
| NM_080632 | UPF3B | NP_542199 | Homo sapiens UPF3 regulator of nonsense transcripts homolog B (yeast) (UPF3B), transcript variant 1, mRNA |

Figure 14

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | | | Description |
|---|---|---|---|---|---|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | |
| AB002310 | KIAA0312 | BAA20771 | | | Homo sapiens mRNA for KIAA0312 gene, partial cds. |
| NM_001005 | RPS3 | NP_000996 | | | Homo sapiens ribosomal protein S3 (RPS3), mRNA. |
| NM_016638 | ARL6IP4 | NP_057722 | | | Homo sapiens ADP-ribosylation-like factor 6 interacting protein 4 (ARL6IP4), mRNA. |
| NM_018387 | STRBP | NP_060857 | | | Homo sapiens spermatid perinuclear RNA binding protein (STRBP), mRNA. |
| NM_001212 | C1QBP | NP_001203 | | | Homo sapiens complement component 1, q subcomponent binding protein (C1QBP), nuclear gene encoding mitochondrial protein, mRNA. |
| NM_004985 | KRAS2 | NP_004976 | | | Homo sapiens v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene homolog (KRAS2), transcript variant b, mRNA. |
| XM_061002 | LOC118523 | XP_061002 | | | Homo sapiens LOC118523 (LOC118523), mRNA. |
| NM_003799 | RNMT | NP_003790 | | | Homo sapiens RNA (guanine-7-) methyltransferase (RNMT), mRNA. |
| NM_021190 | PTBP2 | NP_067013 | | | Homo sapiens polypyrimidine tract binding protein 2 (PTBP2), mRNA. |
| NM_030980 | FLJ12671 | NP_112242 | | | Homo sapiens hypothetical protein FLJ12671 (FLJ12671), mRNA. |
| NM_000971 | RPL7 | NP_000962 | | | Homo sapiens ribosomal protein L7 (RPL7), mRNA. |
| NM_000995 | RPL34 | NP_000986 | | | Homo sapiens ribosomal protein L34 (RPL34), transcript variant 1, mRNA. |
| NM_007006 | CPSF5 | NP_008937 | | | Homo sapiens cleavage and polyadenylation specific factor 5, 25 kDa (CPSF5), mRNA. |
| NM_003429 | ZNF85 | NP_003420 | | | Homo sapiens zinc finger protein 85 (HNF4, HTF1) (ZNF85), mRNA. |
| NM_006112 | PPIE | NP_006103 | | | Homo sapiens peptidylprolyl isomerase E (cyclophilin E) (PPIE), transcript variant 1, mRNA. |
| NM_014502 | PRP19 | NP_055317 | | | Homo sapiens PRP19/PSO4 homolog (S. cerevisiae) (PRP19), mRNA. |
| AC004858 | WUGSC:H_DJ0687K01.2 | AAF19255 | | | Homo sapiens PAC clone RP4-687K1 from 14, complete sequence. |
| XM_060358 | LOC127164 | XP_060358 | | | Homo sapiens similar to TAR DNA binding protein (LOC127164), mRNA. |
| NM_003819 | PABPC4 | NP_003810 | | | Homo sapiens poly(A) binding protein, cytoplasmic 4 (inducible form) (PABPC4), mRNA. |
| AB014564 | KIAA0664 | BAA31639 | | | Homo sapiens mRNA for KIAA0664 protein, partial cds. |
| NM_022170 | WBSOR1 | NP_071496 | | | Homo sapiens Williams-Beuren syndrome chromosome region 1 (WBSOR1), transcript variant 1, mRNA. |
| NM_005087 | FXR1 | NP_005078 | | | Homo sapiens fragile X mental retardation, autosomal homolog 1 (FXR1), mRNA. |
| NM_003680 | YARS | NP_003671 | | | Homo sapiens tyrosyl-tRNA synthetase (YARS), mRNA. |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | | | Description |
|---|---|---|---|---|---|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | |
| NM_004500 | HNRPC | NP_004491 | | | Homo sapiens heterogeneous nuclear ribonucleoprotein C (C1/C2) (HNRPC), transcript variant 2, mRNA. |
| AC004858 | WUGSCH_DJ0687K01.2 | AAF19255 | | | Homo sapiens PAC clone RP4-687K1 from 14, complete sequence. |
| NM_002887 | RARS | NP_002878 | | | Homo sapiens arginyl-tRNA synthetase (RARS), mRNA. |
| NM_020414 | DDX24 | NP_055147 | | | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 24 (DDX24), mRNA. |
| NM_014871 | USP52 | NP_055686 | | | Homo sapiens ubiquitin specific protease 52 (USP52), mRNA. |
| XM_063601 | LOC123341 | XP_063601 | | | Homo sapiens similar to Heterogeneous nuclear ribonucleoprotein A1 (Helix-destabilizing protein) (Single-strand binding protein) (hnRNP core protein A1) (HDP) (LOC123341), mRNA. |
| NM_000988 | RPL27 | NP_000979 | | | Homo sapiens ribosomal protein L27 (RPL27), mRNA. |
| AF266720S4 | RBMX | AAK58567 | | | Homo sapiens RBMX (RBMX) gene, exons 6 through 9 and complete cds. |
| NM_001967 | EIF4A2 | NP_001958 | | | Homo sapiens eukaryotic translation initiation factor 4A, isoform 2 (EIF4A2), mRNA. |
| XM_059612 | LOC132928 | XP_059612 | | | Homo sapiens similar to polyA binding protein (AA 1-633) (LOC132928), mRNA. |
| NM_018959 | DAZAP1 | NP_081832 | | | Homo sapiens DAZ associated protein 1 (DAZAP1), transcript variant 2, mRNA. |
| NM_004294 | MTRF1 | NP_004285 | | | Homo sapiens mitochondrial translational release factor 1 (MTRF1), nuclear gene encoding mitochondrial protein, mRNA. |
| NM_001031 | RPS28 | NP_001022 | | | Homo sapiens ribosomal protein S28 (RPS28), mRNA. |
| AB046830 | KIAA1610 | BAB13436 | | | Homo sapiens mRNA for KIAA1610 protein, partial cds. |
| NM_007358 | M96 | NP_031384 | | | Homo sapiens likely ortholog of mouse metal response element binding transcription factor 2 (M96), mRNA. |
| AF083441 | | AAD52028 | | | Homo sapiens SU11 Isolog mRNA, complete cds. |
| NM_014393 | STAU2 | NP_055208 | | | Homo sapiens stauflin, RNA binding protein, homolog 2 (Drosophila) (STAU2), mRNA. |
| NM_017544 | NRF | NP_060014 | | | Homo sapiens NF-kappa B-repressing factor (NRF), mRNA. |
| AF155096 | | AAD42862 | | | Homo sapiens NY-REN-6 antigen mRNA, partial cds. |
| NM_015703 | CGI-96 | NP_056518 | | | Homo sapiens CGI-96 protein (CGI-96), mRNA. |
| NM_021993 | FUSIP2 | NP_068833 | | | Homo sapiens FUS interacting protein (serine-arginine rich) 2 (FUSIP2), mRNA. |
| NM_001970 | EIF5A | NP_001961 | | | Homo sapiens eukaryotic translation initiation factor 5A (EIF5A), mRNA. |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | |
|---|---|---|---|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | Description |
| NM_012322 | LSM5 | NP_036454 | Homo sapiens LSM5 homolog, U6 small nuclear RNA associated (S. cerevisiae) (LSM5), mRNA |
| NM_003142 | SSB | NP_003133 | Homo sapiens Sjogren syndrome antigen B (autoantigen La) (SSB), mRNA |
| NM_003017 | SFRS3 | NP_003008 | Homo sapiens splicing factor, arginine/serine-rich 3 (SFRS3), mRNA |
| AC004957 | | | Homo sapiens PAC clone RP5-1093O17 from 7, complete sequence. |
| NM_001019 | RPS15A | NP_001010 | Homo sapiens ribosomal protein S15a (RPS15A), mRNA |
| NM_005782 | THOC4 | NP_005773 | Homo sapiens THO complex 4 (THOC4), mRNA |
| NM_006924 | SFRS1 | NP_006855 | Homo sapiens splicing factor, arginine/serine-rich 1 (splicing factor 2, alternate splicing factor) (SFRS1), mRNA |
| NM_031369 | HNRPD | NP_112737 | Homo sapiens heterogeneous nuclear ribonucleoprotein D (AU-rich element RNA binding protein 1, 37kDa) (HNRPD), transcript variant 2, mRNA |
| NM_020690 | MASK | NP_065741 | Homo sapiens multiple ankyrin repeats, single KH-domain (MASK) homolog (MASK), mRNA |
| NM_016047 | P14 | NP_057131 | Homo sapiens pre-mRNA branch site protein p14 (P14), mRNA |
| NM_004953 | EIF4G1 | NP_004944 | Homo sapiens eukaryotic translation initiation factor 4 gamma, 1 (EIF4G1), transcript variant 5, mRNA |
| NM_006625 | FUSIP1 | NP_006616 | Homo sapiens FUS interacting protein (serine-arginine rich) 1 (FUSIP1), transcript variant 1, mRNA |
| NM_021104 | RPL41 | NP_066927 | Homo sapiens ribosomal protein L41 (RPL41), mRNA |
| NM_001751 | CARS | NP_001742 | Homo sapiens cysteinyl-tRNA synthetase (CARS), transcript variant 2, mRNA |
| NM_001533 | HNRP1 | NP_001524 | Homo sapiens heterogeneous nuclear ribonucleoprotein L (HNRP1), mRNA |
| NM_004397 | DDX6 | NP_004388 | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 6 (DDX6), mRNA |
| NM_005762 | TRIM28 | NP_005753 | Homo sapiens tripartite motif-containing 28 (TRIM28), mRNA |
| NM_003756 | EIF3S3 | NP_003747 | Homo sapiens eukaryotic translation initiation factor 3, subunit 3 gamma, 40kDa (EIF3S3), mRNA |
| NM_022551 | RPS18 | NP_072045 | Homo sapiens ribosomal protein S18 (RPS18), mRNA |
| NM_020365 | EIF2B3 | NP_065098 | Homo sapiens eukaryotic translation initiation factor 2B, subunit 3 gamma, 58kDa (EIF2B3), mRNA |
| XM_047499 | LOC149603 | XP_047499 | Homo sapiens hypothetical protein LOC149603 (LOC149603), mRNA |
| NM_006548 | IMP-2 | NP_006539 | Homo sapiens IGF-II mRNA-binding protein 2 (IMP-2), mRNA |
| NM_000984 | RPL23A | NP_000975 | Homo sapiens ribosomal protein L23a (RPL23A), mRNA |

| Nucleotide | | Protein Product | |
|--|--------------------------------------|--|--|
| GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | GeneBank Accession Number or Manufacturer Sequence Reference | Description |
| NM_001022 | RPS19 | NP_001013 | Homo sapiens ribosomal protein S19 (RPS19), mRNA. |
| NM_005617 | RPS14 | NP_005608 | Homo sapiens ribosomal protein S14 (RPS14), mRNA. |
| NM_003187 | TAF9 | NP_003178 | Homo sapiens TAF9 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 32kDa (TAF9), transcript variant 1, mRNA. |
| NM_006386 | DDX17 | NP_006377 | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 17 (DDX17), transcript variant 1, mRNA. |
| NM_000990 | RPL27A | NP_000981 | Homo sapiens ribosomal protein L27a (RPL27A), mRNA. |
| NM_005850 | SF3B4 | NP_005841 | Homo sapiens splicing factor 3b, subunit 4, 49kDa (SF3B4), mRNA. |
| AC004957 | | | Homo sapiens PAC clone RP5-1093O17 from 7, complete sequence. |
| NM_003729 | RTCD1 | NP_003720 | Homo sapiens RNA terminal phosphate cyclase domain 1 (RTCD1), mRNA. |
| NM_006451 | PAIP1 | NP_006442 | Homo sapiens poly(A) binding protein interacting protein 1 (PAIP1), transcript variant 1, mRNA. |
| NM_002137 | HNRPA2B1 | NP_002128 | Homo sapiens heterogeneous nuclear ribonucleoprotein A2/B1 (HNRPA2B1), transcript variant A2, mRNA. |
| NM_001009 | RPS5 | NP_001000 | Homo sapiens ribosomal protein S5 (RPS5), mRNA. |
| NM_005646 | TARBP1 | NP_005637 | Homo sapiens TAR (HIV) RNA binding protein 1 (TARBP1), mRNA. |
| NM_015646 | RAP1B | NP_056461 | Homo sapiens RAP1B, member of RAS oncogene family (RAP1B), mRNA. |
| XM_064113 | LOC124380 | XP_064113 | Homo sapiens LOC124380 (LOC124380), mRNA. |
| NM_004697 | PRPF4 | NP_004688 | Homo sapiens PRP4 pre-mRNA processing factor 4 homolog (yeast) (PRPF4), mRNA. |
| AC004957 | | | Homo sapiens PAC clone RP5-1093O17 from 7, complete sequence. |
| NM_001358 | DXH15 | NP_001349 | Homo sapiens PAC clone RP5-1093O17 from 7, complete sequence. |
| NM_005520 | HNRPH1 | NP_005511 | Homo sapiens DEAD (Asp-Glu-Ala-His) box polypeptide 15 (DXH15), mRNA. |
| NM_003333 | UBA52 | NP_003324 | Homo sapiens heterogeneous nuclear ribonucleoprotein H1 (H) (HNRPH1), mRNA. |
| XM_098297 | LOC153028 | XP_098297 | Homo sapiens ubiquitin A-52 residue ribosomal protein fusion product 1 (UBA52), mRNA. |
| NM_006559 | KHDRBS1 | NP_006550 | Homo sapiens similar to RNA binding protein S1, serine-rich domain (H. sapiens) (LOC153028), mRNA. |
| BC000595 | DDX17 | AAH00595 | Homo sapiens KH domain containing, RNA binding, signal transduction associated 1 (KHDRBS1), mRNA. |
| | | | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 17, mRNA (cDNA clone MGC:3345982), complete cds. |
| NM_001006 | RPS3A | NP_000997 | Homo sapiens ribosomal protein S3A (RPS3A), mRNA. |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | | | Description |
|---|---|---|---|---|---|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | |
| NM_005870 | SAP18 | NP_005861 | | | Homo sapiens sin3-associated polypeptide, 18kDa (SAP18), mRNA. |
| NM_014412 | SIP | NP_055227 | | | Homo sapiens Siah1-interacting protein (SIP), mRNA. |
| NM_007104 | RPL10A | NP_009035 | | | Homo sapiens ribosomal protein L10a (RPL10A), mRNA. |
| NM_005121 | THRAP1 | NP_051112 | | | Homo sapiens thyroid hormone receptor associated protein 1 (THRAP1), mRNA. |
| NM_080663 | MGC16943 | NP_542394 | | | Homo sapiens similar to RIKEN cDNA 4933424N09 gene (MGC16943), mRNA. |
| NM_006074 | TRIM22 | NP_006065 | | | Homo sapiens tripartite motif-containing 22 (TRIM22), mRNA. |
| NM_002950 | RPN1 | NP_002941 | | | Homo sapiens ribophorin I (RPN1), mRNA. |
| XM_062934 | LOC122056 | XP_082934 | | | Homo sapiens similar to ATP-dependent RNA helicase A (Nuclear DNA helicase II) (NDH II) (DEAD-box protein 9) (LOC122056), mRNA. |
| NM_033117 | RBM18 | NP_149108 | | | Homo sapiens RNA binding motif protein 18 (RBM18), mRNA. |
| NM_005034 | POLR2K | NP_005025 | | | Homo sapiens polymerase (RNA) II (DNA directed) polypeptide K, 7.0kDa (POLR2K), mRNA. |
| NM_006805 | HNRPAD | NP_006796 | | | Homo sapiens heterogeneous nuclear ribonucleoprotein A0 (HNRPAD), mRNA. |
| NM_002696 | POLR2G | NP_002687 | | | Homo sapiens polymerase (RNA) II (DNA directed) polypeptide G (POLR2G), mRNA. |
| NM_002140 | HNRPK | NP_002131 | | | Homo sapiens heterogeneous nuclear ribonucleoprotein K (HNRPK), transcript variant 1, mRNA. |
| XM_053153 | LOC149973 | XP_053153 | | | Homo sapiens similar to RNA binding motif protein, X chromosome (H. sapiens) (LOC149973), mRNA. |
| XM_070603 | LOC137784 | XP_070603 | | | Homo sapiens similar to ANTIGEN GOR (LOC137784), mRNA. |
| NM_002938 | RNF4 | NP_002929 | | | Homo sapiens ring finger protein 4 (RNF4), mRNA. |
| XM_086419 | LOC149092 | XP_086419 | | | Homo sapiens similar to pumilio homolog 1 (Drosophila) (H. sapiens) (LOC149092), mRNA. |
| AC004957 | | | | | Homo sapiens PAC clone RP5-1093O17 from 7, complete sequence. |
| NM_002520 | NPM1 | NP_002511 | | | Homo sapiens nucleophosmin (nucleolar phosphoprotein B23, numatrin) (NPM1), mRNA. |
| NM_005437 | NCOA4 | NP_005428 | | | Homo sapiens nuclear receptor coactivator 4 (NCOA4), mRNA. |
| NM_001000 | RPL39 | NP_000991 | | | Homo sapiens ribosomal protein L39 (RPL39), mRNA. |
| NM_000969 | RPL5 | NP_000960 | | | Homo sapiens ribosomal protein L5 (RPL5), mRNA. |
| NM_000973 | RPL8 | NP_000964 | | | Homo sapiens ribosomal protein L8 (RPL8), transcript variant 1, mRNA. |
| NM_003651 | CSDA | NP_003642 | | | Homo sapiens cold shock domain protein A (CSDA), mRNA. |

Figure 14

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | | Description |
|---|---|---|---------------------------|--|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | Manufacturer Reference | |
| XM_067918 | LOC132583 | XP_067918 | | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 (HELIX-DESTABILIZING PROTEIN) (SINGLE-STRAND BINDING PROTEIN) (HNRNP CORE PROTEIN A1) (LOC132583), mRNA. |
| NM_006450 | SPF45 | NP_006441 | | Homo sapiens splicing factor (45kD) (SPF45), mRNA. |
| NM_014912 | CPEB3 | NP_055727 | | Homo sapiens cytoplasmic polyadenylation element binding protein 3 (CPEB3), mRNA. |
| NM_001326 | CSTF3 | NP_001317 | | Homo sapiens cleavage stimulation factor, 3' pre-RNA, subunit 3, 77kDa (CSTF3), mRNA. |
| NM_004940 | DDX7 | NP_004931 | | Homo sapiens DEAD/HA (Asp-Glu-Ala-Asp/His) box polypeptide 7 (RNA helicase, 52kDa) (DDX7), mRNA. |
| NM_005021 | ENPP3 | NP_005012 | | Homo sapiens ectonucleotide pyrophosphatase/phosphodiesterase 3 (ENPP3), mRNA. |
| NM_006047 | RBM12 | NP_006038 | | Homo sapiens RNA binding motif protein 12 (RBM12), transcript variant 1, mRNA. |
| NM_014676 | PUM1 | NP_055491 | | Homo sapiens pumilio homolog 1 (Drosophila) (PUM1), mRNA. |
| NM_002786 | PSMA1 | NP_002777 | | Homo sapiens proteasome (prosome, macropain) subunit, alpha type, 1 (PSMA1), transcript variant 2, mRNA. |
| HUMNUCTIAR | | AAA36384 | | Homo sapiens nucleolysin TIAR mRNA, complete cds. |
| XM_086011 | LOC148027 | XP_086011 | | Homo sapiens similar to bruno-like 5, RNA binding protein (Drosophila); Bruno (Drosophila) -like 5, RNA binding protein; CUG-BP and ETR-3 like factor 5; RNA-binding protein BRUNOL-5 (LOC148027), mRNA. |
| NM_000967 | RPL3 | NP_000958 | | Homo sapiens ribosomal protein L3 (RPL3), mRNA. |
| NM_014071 | NCOA6 | NP_054790 | | Homo sapiens nuclear receptor coactivator 6 (NCOA6), mRNA. |
| XM_073386 | LOC119594 | XP_073386 | | Homo sapiens similar to SPLICING FACTOR U2AF 65 KDA SUBUNIT (U2 AUXILIARY FACTOR 65 KDA SUBUNIT)/U2 SNRNP AUXILIARY FACTOR LARGE SUBUNIT (U2AF65) (LOC119594), mRNA. |
| NM_000982 | RPL21 | NP_000973 | | Homo sapiens ribosomal protein L21 (RPL21), mRNA. |
| AF062105 | IGH | AAC18141 | | Homo sapiens clone 21u-19 immunoglobulin heavy chain variable region (IGH) mRNA, partial cds. |
| NM_006414 | RPP38 | NP_006405 | | Homo sapiens ribonuclease P/MRP 38kDa subunit (RPP38), transcript variant 2, mRNA. |
| NM_004599 | SREBF2 | NP_004590 | | Homo sapiens sterol regulatory element binding transcription factor 2 (SREBF2), mRNA. |
| NM_007273 | REA | NP_009204 | | Homo sapiens repressor of estrogen receptor activity (REA), mRNA. |
| NM_002453 | MTIF2 | NP_002444 | | Homo sapiens mitochondrial translational initiation factor 2 (MTIF2), nuclear gene encoding mitochondrial protein, mRNA. |

Figure 14

| Nucleotide | | | Protein Product | | |
|-------------------|---------------------------|-------------|---------------------------|--------------------|--|
| GenBank Accession | Gene Name or Manufacturer | Sequence ID | Gene Name or Manufacturer | Sequence Reference | Description |
| AF380184 | SON | | | AAL34502 | Homo sapiens SON DNA binding protein isoform F (SON) mRNA, complete cds, alternatively spliced. |
| HUMRNAHELA | DDX9 | | | AAB48855 | Human RNA helicase A mRNA, complete cds. |
| NM_006929 | SKIV2L | | | NP_008860 | Homo sapiens superkiller virulicidal activity 2-like (S. cerevisiae) (SKIV2L), mRNA. |
| AK001652 | | | | BAA91812 | Homo sapiens cDNA FLJ10790 fis, clone NT2RP4000518, weakly similar to ATP-DEPENDENT RNA HELICASE ROK1. |
| AF037448 | GRY-RBP | | | AAC12926 | Homo sapiens RRM RNA binding protein Gry-rbp (GRY-RBP) mRNA, complete cds. |
| NM_000977 | RPL13 | | | NP_000968 | Homo sapiens ribosomal protein L13 (RPL13), transcript variant 1, mRNA. |
| NM_016024 | CGI-79 | | | NP_057108 | Homo sapiens CGI-79 protein (CGI-79), mRNA. |
| AB044971 | nopp34 | | | BAB41210 | Homo sapiens mRNA for nucleolar phosphoprotein Nopp34, complete cds. |
| NM_000996 | RPL35A | | | NP_000987 | Homo sapiens ribosomal protein L35a (RPL35A), mRNA. |
| NM_031277 | RNF17 | | | NP_112567 | Homo sapiens ring finger protein 17 (RNF17), transcript variant long, mRNA. |
| XM_067051 | LOC140065 | | | XP_067051 | Homo sapiens similar to RNA binding motif protein, Y chromosome, family 1 member A1 (RNA-binding motif protein 1) (LOC140065), mRNA. |
| NM_006276 | SFRS7 | | | NP_006267 | Homo sapiens splicing factor, arginine/serine-rich 7, 35kDa (SFRS7), mRNA. |
| NM_005008 | NHP2L1 | | | NP_004999 | Homo sapiens NHP2 non-histone chromosome protein 2-like 1 (S. cerevisiae) (NHP2L1), mRNA. |
| NM_003138 | SRPK2 | | | NP_003129 | Homo sapiens SFRS protein kinase 2 (SRPK2), mRNA. |
| XM_092386 | LOC165115 | | | XP_092386 | Homo sapiens similar to KIAA1841 protein (LOC165115), mRNA. |
| XM_062047 | LOC120470 | | | XP_062047 | Homo sapiens similar to discs, large (Drosophila) homolog 2; chapsyn-110 (LOC120470), mRNA. |
| NM_000991 | RPL28 | | | NP_000982 | Homo sapiens ribosomal protein L28 (RPL28), mRNA. |
| NM_001537 | HSBP1 | | | NP_001528 | Homo sapiens heat shock factor binding protein 1 (HSBP1), mRNA. |
| AB025254 | | | | BAA76379 | Homo sapiens mRNA for tudor repeat associator with PCTAIRE 2, partial cds. |
| NM_006696 | BRD8 | | | NP_006687 | Homo sapiens bromodomain containing 8 (BRD8), transcript variant 1, mRNA. |
| NM_030941 | LOC81691 | | | NP_112203 | Homo sapiens exonuclease NEF-sp (LOC81691), mRNA. |
| NM_016132 | MYEF2 | | | NP_057216 | Homo sapiens myelin expression factor 2 (MYEF2), mRNA. |
| NM_004640 | BAT1 | | | NP_004631 | Homo sapiens HLA-B associated transcript 1 (BAT1), transcript variant 1, mRNA. |

Figure 11

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | | Description |
|---|---|---|---------------------------------------|---|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | Manufacturer Sequence Reference | |
| NM_012345 | NUFIP1 | NP_036477 | | Homo sapiens nuclear fragile X mental retardation protein interacting protein 1 (NUFIP1), mRNA. |
| XM_092031 | LOC163147 | XP_092031 | | Homo sapiens similar to Splicing factor 3A subunit 2 (Spliceosome associated protein 62) (SAP 62) (SF3a66) (LOC163147), mRNA. |
| XM_067074 | LOC140100 | XP_067074 | | Homo sapiens similar to RBM1 (LOC140100), mRNA. |
| NM_002047 | GARS | NP_002038 | | Homo sapiens glycyl-tRNA synthetase (GARS), mRNA. |
| NM_001017 | RPS13 | NP_001008 | | Homo sapiens ribosomal protein S13 (RPS13), mRNA. |
| NM_004506 | HSF2 | NP_004497 | | Homo sapiens heat shock transcription factor 2 (HSF2), mRNA. |
| NM_012426 | SF3B3 | NP_036558 | | Homo sapiens splicing factor 3b, subunit 3, 130kDa (SF3B3), mRNA. |
| NM_019038 | TDRD4 | NP_061911 | | Homo sapiens tudor domain containing 4 (TDRD4), mRNA. |
| AC022517 | | AAF31271 | | Homo sapiens chromosome 19, BC335474 (CIT-HSPC_482H14), complete sequence. |
| NM_001111 | ADAR | NP_001102 | | Homo sapiens adenosine deaminase, RNA-specific (ADAR), transcript variant ADAR-a, mRNA. |
| XM_060102 | LOC126635 | XP_060102 | | Homo sapiens LOC126635 (LOC126635), mRNA. |
| NM_017803 | FLJ20399 | NP_060273 | | Homo sapiens hypothetical protein FLJ20399 (FLJ20399), mRNA. |
| XM_001524 | LOC151173 | XP_001524 | | Homo sapiens similar to TAR DNA-binding protein-43 (TDP-43) (LOC151173), mRNA. |
| NM_004757 | SCYE1 | NP_004748 | | Homo sapiens small inducible cytokine subfamily E, member 1 (endothelial monocyte-activating) (SCYE1), mRNA. |
| NM_014003 | DHX38 | NP_054722 | | Homo sapiens DEAH (Asp-Glu-Ala-His) box polypeptide 38 (DHX38), mRNA. |
| XM_086792 | LOC150152 | XP_086792 | | Homo sapiens similar to SPLICING FACTOR U2AF 35 KD SUBUNIT (U2 AUXILIARY FACTOR 35 KD SUBUNIT) (U2 SNRNP AUXILIARY FACTOR SMALL SUBUNIT) (LOC150152), mRNA. |
| AC004957 | | | | Homo sapiens PAC clone RPS-1093017 from 7, complete sequence. |
| NM_007007 | CPSF6 | NP_008938 | | Homo sapiens cleavage and polyadenylation specific factor 6, 68kDa (CPSF6), mRNA. |
| NM_019037 | EXOSC4 | NP_061910 | | Homo sapiens exosome component 4 (EXOSC4), mRNA. |
| XM_070605 | LOC137786 | XP_070605 | | Homo sapiens similar to ANTIGEN GOR (LOC137786), mRNA. |
| NM_017736 | FLJ20274 | NP_060206 | | Homo sapiens hypothetical protein FLJ20274 (FLJ20274), mRNA. |
| NM_018046 | HSU84971 | NP_060516 | | Homo sapiens vasculogenesis gene on 5q (HSU84971), mRNA. |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | | | Description |
|---|---|---|---|---|---|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | |
| NM_006842 | SF3B2 | NP_006833 | | | Homo sapiens splicing factor 3b, subunit 2, 145kD (SF3B2), mRNA. |
| NM_021033 | RAP2A | NP_066361 | | | Homo sapiens RAP2A, member of RAS oncogene family (RAP2A), mRNA. |
| XM_095899 | LOC169732 | XP_095899 | | | Homo sapiens similar to EXOSOME COMPLEX EXONUCLEASE RRP4 (RIBOSOMAL RNA PROCESSING PROTEIN 4) (LOC169732), mRNA. |
| NM_031274 | TEX13A | NP_112564 | | | Homo sapiens testis expressed sequence 13A (TEX13A), mRNA. |
| NM_008387 | CHERP | NP_008378 | | | Homo sapiens calcium homeostasis endoplasmic reticulum protein (CHERP), mRNA. |
| NM_000964 | RARA | NP_000955 | | | Homo sapiens retinoic acid receptor, alpha (RARA), mRNA. |
| XM_066446 | LOC139051 | XP_066446 | | | Homo sapiens similar to pol protein (LOC139051), mRNA. |
| NM_003072 | SMARCA4 | NP_003063 | | | Homo sapiens SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4 (SMARCA4), mRNA. |
| NM_022767 | FLJ12484 | NP_073604 | | | Homo sapiens hypothetical protein FLJ12484 (FLJ12484), mRNA. |
| NM_001112 | ADARB1 | NP_001103 | | | Homo sapiens adenosine deaminase, RNA-specific, B1 (RED1 homolog rat) (ADARB1), transcript variant DRADA2a, mRNA. |
| NM_017774 | CDKAL1 | NP_060244 | | | Homo sapiens CDK5 regulatory subunit associated protein 1-like 1 (CDKAL1), mRNA. |
| NM_013302 | EEF2K | NP_037434 | | | Homo sapiens elongation factor-2 kinase (EEF2K), mRNA. |
| NM_018702 | ADARB2 | NP_061172 | | | Homo sapiens adenosine deaminase, RNA-specific, B2 (RED2 homolog rat) (ADARB2), mRNA. |
| XM_089765 | LOC143344 | XP_089765 | | | Homo sapiens similar to poly(A) binding protein (LOC143344), mRNA. |
| AF026564 | RBMI | AAC16916 | | | Homo sapiens RNA binding protein II (RBMI) gene, complete cds. |
| NM_016333 | SRRM2 | NP_057417 | | | Homo sapiens serine/arginine repetitive matrix 2 (SRRM2), mRNA. |
| NM_004039 | ANXA2 | NP_004030 | | | Homo sapiens annexin A2 (ANXA2), mRNA. |
| NM_006187 | OAS3 | NP_006178 | | | Homo sapiens 2'-5'-oligoadenylate synthetase 3, 100kDa (OAS3), mRNA. |
| XM_089587 | LOC159428 | XP_089587 | | | Homo sapiens similar to EUKARYOTIC TRANSLATION INITIATION FACTOR 4B (EIF-4B) (LOC159428), mRNA. |
| AB061839 | RPS9 | BAB79477 | | | Homo sapiens RPS9 gene for ribosomal protein S9, complete cds and sequence. |
| NM_018060 | FLJ10326 | NP_060530 | | | Homo sapiens mitochondrial isoleucine tRNA synthetase (FLJ10326), mRNA. |

Figure 14

| Nucleotide GenBank Accession | | Protein Product | |
|---------------------------------|---|---|--|
| Number or Manufacturer | Gene Name or Manufacturer Probe Name | GeneBank Accession Number or Manufacturer Sequence Reference | Description |
| NM_003787 | NOL4 | NP_003778 | Homo sapiens nucleolar protein 4 (NOL4), mRNA. |
| NM_003086 | SNAPC4 | NP_003077 | Homo sapiens small nuclear RNA activating complex, polypeptide 4, 190kDa (SNAPC4), mRNA. |
| NM_004728 | DDX21 | NP_004719 | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 21 (DDX21), mRNA. |
| XM_092043 | LOC163160 | XP_092043 | Homo sapiens similar to polypyrimidine tract binding protein, isoform b; heterogeneous nuclear ribonucleoprotein polypeptide 1; RNA binding protein (LOC163160), mRNA. |
| NM_014829 | DDX46 | NP_055644 | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 46 (DDX46), mRNA. |
| NM_004597 | SNRPD2 | NP_004588 | Homo sapiens small nuclear ribonucleoprotein D2 polypeptide 16.5kDa (SNRPD2), transcript variant 1, mRNA. |
| NM_004774 | PPARBP | NP_004765 | Homo sapiens PPAR binding protein (PPARBP), mRNA. |
| NM_002515 | NOVA1 | NP_002506 | Homo sapiens neuro-oncological ventral antigen 1 (NOVA1), transcript variant 1, mRNA. |
| NM_006410 | HTATIP2 | NP_006401 | Homo sapiens HIV-1 Tat interactive protein 2, 30kDa (HTATIP2), mRNA. |
| NM_005687 | FARSLB | NP_005678 | Homo sapiens phenylalanine-tRNA synthetase-like, beta subunit (FARSLB), mRNA. |
| NM_001644 | APOBEC1 | NP_001635 | Homo sapiens apolipoprotein B mRNA editing enzyme, catalytic polypeptide 1 (APOBEC1), transcript variant 1, mRNA. |
| NM_033246 | PML | NP_150249 | Homo sapiens promyelocytic leukemia (PML), transcript variant 7, mRNA. |
| XM_091270 | LOC161983 | XP_091270 | Homo sapiens similar to Heterogeneous nuclear ribonucleoprotein A1 (Helix-destabilizing protein) (Single-strand binding protein) (hnRNP core protein A1) (HDP-1) (Topoisomerase-inhibitor suppressed) (LOC161983), mRNA. |
| NM_015409 | EP400 | NP_056224 | Homo sapiens E1A binding protein p400 (EP400), mRNA. |
| NM_015453 | DKFZP434F091 | NP_056268 | Homo sapiens DKFZP434F091 protein (DKFZP434F091), mRNA. |
| XM_067072 | LOC140098 | XP_067072 | Homo sapiens similar to RBM1 (LOC140098), mRNA. |
| XM_056568 | LOC147774 | XP_056568 | Homo sapiens similar to KH-type splicing regulatory protein (FUSE binding protein 2) (H. sapiens) (LOC147774), mRNA. |
| NM_022078 | FLJ12455 | NP_071361 | Homo sapiens hypothetical protein FLJ12455 (FLJ12455), mRNA. |
| NM_001364 | DLG2 | NP_001355 | Homo sapiens discs, large homolog 2, chapsyn-110 (Drosophila) (DLG2), mRNA. |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | |
|---|---|---|---|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | Description |
| NM_003752 | EIF3S8 | NP_003743 | Homo sapiens eukaryotic translation initiation factor 3, subunit 8, 110kDa (EIF3S8), mRNA |
| XM_091235 | LOC161931 | XP_091235 | Homo sapiens similar to testis nuclear RNA binding protein; testis nuclear RNA-binding protein (LOC161931), mRNA. |
| NM_014977 | ACINUS | NP_055792 | Homo sapiens apoptotic chromatin condensation inducer in the nucleus (ACINUS), mRNA. |
| NM_000461 | THRB | NP_000452 | Homo sapiens thyroid hormone receptor, beta (erythroblastic leukemia viral (v-erb-a) oncogene homolog 2, avian) (THRB), mRNA. |
| NM_024939 | FLJ21918 | NP_079215 | Homo sapiens hypothetical protein FLJ21918 (FLJ21918), mRNA. |
| NM_032572 | RNASE7 | NP_115961 | Homo sapiens ribonuclease, RNase A family, 7 (RNASE7), mRNA. |
| AF315592 | PUMH1 | AAG31807 | Homo sapiens Pumilio 1 (PUMH1) mRNA, complete cds. |
| NM_004433 | ELF3 | NP_004424 | Homo sapiens E74-like factor 3 (ets domain transcription factor, epithelial-specific) (ELF3), mRNA. |
| XM_058943 | LOC125925 | XP_058943 | Homo sapiens similar to R32611_1 (LOC125925), mRNA. |
| NM_006624 | BS69 | NP_006615 | Homo sapiens adenovirus 5 E1A binding protein (BS69), mRNA. |
| NM_016166 | PIAS1 | NP_057250 | Homo sapiens protein inhibitor of activated STAT, 1 (PIAS1), mRNA. |
| NM_006663 | RAI | NP_006654 | Homo sapiens RelA-associated inhibitor (RAI), mRNA. |
| XM_058876 | MGC49942 | XP_058876 | Homo sapiens hypothetical protein MGC49942 (MGC49942), mRNA. |
| NM_000057 | BLM | NP_000048 | Homo sapiens Bloom syndrome (BLM), mRNA. |
| NM_004461 | FARSLA | NP_004452 | Homo sapiens phenylalanine-tRNA synthetase-like, alpha subunit (FARSLA), mRNA. |
| NM_006163 | NFE2 | NP_006154 | Homo sapiens nuclear factor (erythroid-derived 2), 45kDa (NFE2), mRNA. |
| AE006640 | NDUFB10 | AAK61302 | Homo sapiens 16p13.3 sequence section 8 of 8. |
| NM_017846 | SECP43 | NP_060316 | Homo sapiens tRNA selenocysteine associated protein (SECP43), mRNA. |
| XM_088975 | LOC148683 | XP_088975 | Homo sapiens similar to pumilio homolog 1 (Drosophila); pumilio (Drosophila) homolog 1 (LOC148683), mRNA. |
| NM_012321 | LSM4 | NP_036453 | Homo sapiens LSM4 homolog, U6 small nuclear RNA associated (S. cerevisiae) (LSM4), mRNA. |
| NM_012143 | TFIP11 | NP_036275 | Homo sapiens tuffin interacting protein 11 (TFIP11), mRNA. |
| NM_001111 | ADAR | NP_001102 | Homo sapiens adenosine deaminase, RNA-specific (ADAR), transcript variant ADAR-a, mRNA. |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | | | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | | Gene Name or Manufacturer Probe Name | | Description |
|---|-----------|-----------|--|-----------|---|------------------------------|--|
| NM_001535 | NM_016173 | NM_005754 | NP_001526 | NP_057257 | NP_005745 | HRMT1L1 HEMK G3BP | Homo sapiens HMT1 hnRNP methyltransferase-like 1 (<i>S. cerevisiae</i>) (HRMT1L1), mRNA. Homo sapiens HEMK homolog 7kb (HEMK), mRNA. Homo sapiens Ras-GTPase-activating protein SH3-domain-binding protein (G3BP), transcript variant 1, mRNA |
| NM_002892 | XM_092221 | NM_001412 | NP_002883 | XP_092221 | NP_001403 | ARID4A LOC164891 EIF1A | Homo sapiens AT rich interactive domain 4A (RBP1-like) (ARID4A), transcript variant 1, mRNA. Homo sapiens similar to mRNA for ribosomal protein S9 (LOC164891), mRNA. Homo sapiens eukaryotic translation initiation factor 1A (EIF1A), mRNA |
| XM_095591 | | XM_095591 | XP_095591 | | XP_095591 | LOC169242 | Homo sapiens similar to data source:SPT, source key:O94865, evidence:ISS-homolog to KIAA0765 PROTEIN (HRIHFB2091 PROTEIN) (FRAGMENT)-putative (LOC169242), mRNA. |
| NM_033004 | XM_093336 | NM_012255 | NP_127497 | XP_093336 | NP_036387 | NALP1 LOC165631 XRN2 | Homo sapiens NACHT, leucine rich repeat and PYD containing 1 (NALP1), transcript variant 1, mRNA. Homo sapiens similar to Eukaryotic translation initiation factor 4B (eIF-4B) (LOC165631), mRNA. Homo sapiens 5'-3' exoribonuclease 2 (XRN2), mRNA. |
| XM_065002 | XM_065002 | NM_001618 | XP_065002 | XP_065002 | NP_001609 | LOC126246 ADPRT | Homo sapiens LOC126246 (LOC126246), mRNA. Homo sapiens ADP-ribosyltransferase (NAD ⁺ ; poly (ADP-ribose) polymerase) (ADPRT), mRNA. |
| XM_087452 | | XM_087452 | XP_087452 | | XP_087452 | LOC131596 | Homo sapiens similar to splicing factor 3a, subunit 2, 66kD; Spliceosome protein SAP-62 (LOC131596), mRNA. |
| XM_062601 | HUMAUA | NM_001686 | XP_062601 | AAB59352 | NP_001677 | LOC121365 ATP5B | Homo sapiens similar to RBM1 (LOC121365), mRNA. Homo sapiens (clone JH4B1) PM-scl autoantigen mRNA, complete cds. Homo sapiens ATP synthase, H ⁺ transporting, mitochondrial F1 complex, beta polypeptide (ATP5B), mRNA. |
| NM_007294 | NM_002502 | | NP_009225 | NP_009225 | NP_002493 | BRCA1 NFKB2 | Homo sapiens breast cancer 1, early onset (BRCA1), transcript variant BRCA1a, mRNA. Homo sapiens nuclear factor of kappa light polypeptide gene enhancer in B-cells 2 (p49/p100) (NFKB2), mRNA. |
| XM_068248 | NM_021724 | NM_016374 | XP_068248 | NP_068370 | NP_057458 | LOC133225 NR1D1 ARID4B | Homo sapiens similar to heterogeneous ribonuclear particle protein A1.beta - human (LOC133225), mRNA. Homo sapiens nuclear receptor subfamily 1, group D, member 1 (NR1D1), mRNA. Homo sapiens AT rich interactive domain 4B (RBP1- like) (ARID4B), transcript variant1 1, mRNA. |

| Nucleotide | | Protein Product | |
|-------------------|--------------|-----------------|---|
| GenBank Accession | Gene Name or | GeneBank | Description |
| Number or | Manufacturer | Accession | |
| Manufacturer | Sequence | Number or | |
| Sequence ID | Manufacturer | Sequence | |
| Sequence ID | Manufacturer | Sequence | |
| XM_068022 | LOC132772 | XP_068022 | Homo sapiens similar to split ends; polycephalon; yippee interacting protein 1 (LOC132772), mRNA. |
| NM_005548 | KARS | NP_005539 | Homo sapiens lysyl-tRNA synthetase (KARS), mRNA. |
| NM_006311 | NCOR1 | NP_006302 | Homo sapiens nuclear receptor co-repressor 1 (NCOR1), mRNA. |
| NM_016505 | PS1D | NP_057589 | Homo sapiens putative S1 RNA binding domain protein (PS1D), mRNA. |
| NM_004719 | SFRS2IP | NP_004710 | Homo sapiens splicing factor, arginine/serine-rich 2, interacting protein (SFRS2IP), mRNA. |
| NM_003686 | EXO1 | NP_003677 | Homo sapiens exonuclease 1 (EXO1), transcript variant 3, mRNA. |
| NM_005481 | THRAP5 | NP_005472 | Homo sapiens thyroid hormone receptor associated protein 5 (THRAP5), mRNA. |
| NM_002296 | LBR | NP_002287 | Homo sapiens lamin B receptor (LBR), transcript variant 1, mRNA. |
| NM_014966 | DHX30 | NP_055781 | Homo sapiens DEAH (Asp-Glu-Ala-His) box polypeptide 30 (DHX30), transcript variant 2, mRNA. |
| AF026126 | HNRPD | AAC23478 | Homo sapiens heterogeneous nuclear ribonucleoprotein D (HNRPD) gene, complete cds. |
| XM_066901 | LOC139801 | XP_066901 | Homo sapiens LOC139801 (LOC139801), mRNA. |
| AK057303 | | BAB71416 | Homo sapiens cDNA FLJ32741 fis, clone TEST12001345, highly similar to M.musculus Tetr mRNA for RNA binding protein |
| XM_067087 | LOC140123 | XP_067087 | Homo sapiens similar to RNA binding motif protein, Y chromosome, family 2 member B (LOC140123), mRNA. |
| NM_033502 | TRERF1 | NP_277037 | Homo sapiens transcriptional regulating factor 1 (TRERF1), transcript variant 1, mRNA. |
| NM_005822 | DSCR1L1 | NP_005813 | Homo sapiens Down syndrome critical region gene 1-like 1 (DSCR1L1), mRNA. |
| NM_002897 | RBMS1 | NP_002888 | Homo sapiens RNA binding motif, single stranded interacting protein 1 (RBMS1), transcript variant 2, mRNA. |
| XM_067844 | LOC132430 | XP_067844 | Homo sapiens similar to Polyadenylate-binding protein 4 (Poly(A)-binding protein 4) (PABP 4) (Inducible poly(A)-binding protein) (PABP) (Activated-platelet protein-1) (APP-1) (LOC132430), mRNA. |
| NM_002949 | MRPL12 | NP_002940 | Homo sapiens mitochondrial ribosomal protein L12 (MRPL12), nuclear gene encoding mitochondrial protein, mRNA. |
| NM_003219 | TERT | NP_003210 | Homo sapiens telomerase reverse transcriptase (TERT), transcript variant 1, mRNA. |
| XM_070624 | LOC137819 | XP_070624 | Homo sapiens LOC137819 (LOC137819), mRNA. |

| Nucleotide | | | Protein Product | |
|-------------------|--------------|-------------------------|-----------------|--|
| GenBank Accession | Gene Name or | Manufacturer Probe Name | GeneBank | Description |
| Number or | Manufacturer | Manufacturer | Accession | |
| Sequence ID | Manufacturer | Probe Name | Number or | |
| | | | Manufacturer | |
| | | | Sequence | |
| | | | Reference | |
| NM_002937 | RNASE4 | | NP_002928 | Homo sapiens ribonuclease, RNase A family, 4 (RNASE4); transcript variant 2, mRNA. |
| NM_006546 | IMP-1 | | NP_006537 | Homo sapiens IGF-II mRNA-binding protein 1 (IMP-1), mRNA. |
| NM_004860 | FXR2 | | NP_004851 | Homo sapiens fragile X mental retardation, autosomal homolog 2 (FXR2), mRNA. |
| NM_003321 | TUFM | | NP_003312 | Homo sapiens Tu translation elongation factor, mitochondrial (TUFM), mRNA. |
| NM_005693 | NR1H3 | | NP_005684 | Homo sapiens nuclear receptor subfamily 1, group H, member 3 (NR1H3), mRNA. |
| NM_006565 | CTCF | | NP_006556 | Homo sapiens CCCTC-binding factor (zinc finger protein) (CTCF), mRNA. |
| NM_018664 | SNFT | | NP_061134 | Homo sapiens Jun dimerization protein p21SNFT (SNFT), mRNA. |
| M_000938 | POLR2B | | NP_000929 | Homo sapiens polymerase (RNA) II (DNA directed) polypeptide B, 140kDa (POLR2B), mRNA. |
| M_002934 | RNASE2 | | NP_002925 | Homo sapiens ribonuclease, RNase A family, 2 (liver, eosinophil-derived neurotoxin) (RNASE2), mRNA. |
| M_006980 | MTERF | | NP_008911 | Homo sapiens transcription termination factor, mitochondrial (MTERF), nuclear gene encoding mitochondrial protein, mRNA. |

| Gene | | Nucleotide Sequence Description | |
|----------------------------|---------------|---------------------------------|--|
| GenBank Accession for mRNA | Gene Symbol | GenBank Accession for Protein | |
| NM_012070 | ATRN | NP_036202 | Homo sapiens attractin (ATRN), transcript variant 3, mRNA. |
| NM_003488 | AKAP1 | NP_003479 | Homo sapiens A kinase (PRKA) anchor protein 1 (AKAP1), nuclear gene encoding mitochondrial protein, transcript variant 1, mRNA. |
| XM_044795 | LOC92392 | XP_044795 | Homo sapiens similar to colon cancer antigen NY-CO-45 (LOC92392), mRNA. |
| XM_089332 | LOC14938 2 | XP_089332 | Homo sapiens similar to ribosomal protein L22 protein; 60S ribosomal protein L22; Epstein-Barr-encoded RNA-associated protein; Epstein-Barr virus small RNA-associated protein; EBER-associated protein; heparin-binding protein 15; heparin-binding protein HBp15... (LOC149382), mRNA. |
| NM_001024 | RPS21 | NP_001015 | Homo sapiens ribosomal protein S21 (RPS21), mRNA. |
| NM_001324 | CSTF1 | NP_001315 | Homo sapiens cleavage stimulation factor, 3' pre-RNA, subunit 1, 50kDa (CSTF1), mRNA. |
| NM_006625 | FUSIP1 | NP_006616 | Homo sapiens FUS interacting protein (serine-arginine rich) 1 (FUSIP1), transcript variant 1, mRNA. |
| NM_006540 | NCOA2 | NP_006531 | Homo sapiens nuclear receptor coactivator 2 (NCOA2), mRNA. |
| NM_005782 | THOC4 | NP_005773 | Homo sapiens THO complex 4 (THOC4), mRNA. |
| NM_032102 | SRP46 | NP_115285 | Homo sapiens Splicing factor, arginine/serine-rich, 46kD (SRP46), mRNA. |
| NM_014497 | NP220 | NP_055312 | Homo sapiens NP220 nuclear protein (NP220), mRNA. |
| ..._022915 | MRPL44 | NP_075066 | Homo sapiens mitochondrial ribosomal protein L44 (MRPL44), nuclear gene encoding mitochondrial protein, mRNA. |
| _003325 | HIRA | NP_003316 | Homo sapiens HIR histone cell cycle regulation defective homolog A (S. cerevisiae) (HIRA), mRNA. |
| _006397 | RNASEH2A | NP_006388 | Homo sapiens ribonuclease H2, large subunit (RNASEH2A), mRNA. |
| L_006548 | IMP-2 | NP_006539 | Homo sapiens IGF-II mRNA-binding protein 2 (IMP-2), mRNA. |
| L_005801 | SUI1 | NP_005792 | Homo sapiens putative translation initiation factor (SUI1), mRNA. |
| _007157 | | AAC19158 | Homo sapiens clone 23856 unknown mRNA, partial cds. |
| L_000029 | AGT | NP_000020 | Homo sapiens angiotensinogen (serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antitrypsin), member 8) (AGT), mRNA. |
| L_002904 | RDBP | NP_002895 | Homo sapiens RD RNA binding protein (RDBP), mRNA. |
| BC016283 | ABCE1 | AAH16283 | Homo sapiens ATP-binding cassette, sub-family E (OABP), member 1, mRNA (cDNA clone MGC:9023 IMAGE:3909151), complete cds. |
| AF049525 | HYPC | AAC27503 | Homo sapiens huntingtin-interacting protein HYPC (HYPC) mRNA, partial cds. |
| NM_014462 | LSM1 | NP_055277 | Homo sapiens LSM1 homolog, U6 small nuclear RNA associated (S. cerevisiae) (LSM1), mRNA. |

Figure 15

| Gene Symbol | | Nucleotide Sequence Description | |
|----------------------------|-------------------------------|---|--|
| GenBank Accession for mRNA | GenBank Accession for Protein | | |
| AB014564 | KIAA0664 | Homo sapiens mRNA for KIAA0664 protein, partial cds. | |
| NM_001253 | CDC5L | Homo sapiens CDC5 cell division cycle 5-like (S. pombe) (CDC5L), mRNA. | |
| NM_001991 | EZH1 | Homo sapiens enhancer of zeste homolog 1 (Drosophila) (EZH1), mRNA. | |
| NM_001090 | ABCF1 | Homo sapiens ATP-binding cassette, sub-family F (GCN20), member 1 (ABCF1), mRNA. | |
| NM_000061 | BTK | Homo sapiens Bruton agammaglobulinemia tyrosine kinase (BTK), mRNA. | |
| AB020657 | KIAA0850 | Homo sapiens mRNA for KIAA0850 protein, partial cds. | |
| NM_032390 | MKI67IP | Homo sapiens MKI67 (FHA domain) interacting nucleolar phosphoprotein (MKI67IP), mRNA. | |
| NM_030980 | FLJ12671 | Homo sapiens hypothetical protein FLJ12671 (FLJ12671), mRNA. | |
| L_017827 | SARS2 | Homo sapiens seryl-tRNA synthetase 2 (SARS2), mRNA. | |
| L_066948 | LOC139891 | Homo sapiens similar to hypothetical protein BC011593 (LOC139891), mRNA. | |
| L_091974 | LOC147891 | Homo sapiens similar to hypothetical protein DKFZp434i1930 (H. sapiens) (LOC147891), mRNA. | |
| L_014060 | MCTS1 | Homo sapiens malignant T cell amplified sequence 1 (MCTS1), mRNA. | |
| L_000647 | CCR2 | Homo sapiens chemokine (C-C motif) receptor 2 (CCR2), transcript variant A, mRNA. | |
| L_001016 | RPS12 | Homo sapiens ribosomal protein S12 (RPS12), mRNA. | |
| NM_032359 | MGC4308 | Homo sapiens hypothetical protein MGC4308 (MGC4308), mRNA. | |
| NM_017736 | FLJ20274 | Homo sapiens hypothetical protein FLJ20274 (FLJ20274), mRNA. | |
| NM_006627 | POP4 | Homo sapiens processing of precursor 4, ribonuclease P/MRP subunit (S. cerevisiae) (POP4), mRNA. | |
| BC001050 | NFATC3 | Homo sapiens nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 3, transcript variant 1, mRNA (cDNA clone MGC:1495 IMAGE:3505967), complete cds. | |
| NM_000344 | SMN1 | Homo sapiens survival of motor neuron 1, telomeric (SMN1), transcript variant d, mRNA. | |

Figure 16 (1)

| Gene Symbol | GenBank Accession for mRNA | GenBank Accession for Protein | Nucleotide Sequence Description |
|-------------|----------------------------|-------------------------------|---|
| XM_094140 | LOC166863 | XP_094140 | Homo sapiens similar to Apobec-1 complementation factor, APOBEC-1 stimulating protein (LOC166863), mRNA. |
| NM_005548 | KARS | NP_005539 | Homo sapiens lysyl-tRNA synthetase (KARS), mRNA. |
| NM_007235 | XPOT | NP_009166 | Homo sapiens exportin, tRNA (nuclear export receptor for tRNAs) (XPOT), mRNA. |
| AF230402 | | AAG50181 | Homo sapiens tripartite motif protein TRIM19 beta mRNA, complete cds. |
| NM_003680 | YARS | NP_003671 | Homo sapiens tyrosyl-tRNA synthetase (YARS), mRNA. |
| XM_086419 | LOC149092 | XP_086419 | Homo sapiens similar to pumilio homolog 1 (Drosophila) (H. sapiens) (LOC149092), mRNA. |
| NM_015629 | PRPF31 | NP_056444 | Homo sapiens PRP31 pre-mRNA processing factor 31 homolog (yeast) (PRPF31), mRNA. |
| XM_067598 | LOC131898 | XP_067598 | Homo sapiens similar to POLYADENYLATE-BINDING PROTEIN 2 (POLY(A) BINDING PROTEIN 2) (PABP 2) (LOC131898), mRNA. |
| U1255 | EIF2C2 | AAF13034 | Homo sapiens protein translation initiation factor 2C2 (EIF2C2) mRNA, partial cds. |
| U3870 | LOC149816 | XP_086708 | Homo sapiens similar to Splicing factor 3A subunit 3 (Spliceosome associated protein 61) (SAP 61) (SF3a60) (LOC149816), mRNA. |
| U0702 | U1SNRNPBP | NP_008951 | Homo sapiens U1-snRNP binding protein homolog (U1SNRNPBP), transcript variant 1, mRNA. |
| U01745 | STAU | NP_059347 | Homo sapiens staufer, RNA binding protein (Drosophila) (STAU), transcript variant T3, mRNA. |
| U00169 | AUH | NP_001689 | Homo sapiens AU RNA binding protein/enoyl-Coenzyme A hydratase (AUH), nuclear gene encoding mitochondrial protein, mRNA. |
| U00171 | BICD1 | NP_001705 | Homo sapiens Bicaudal D homolog 1 (Drosophila) (BICD1), mRNA. |
| XM_066904 | LOC139804 | XP_066904 | Homo sapiens similar to testes-specific heterogeneous nuclear ribonucleoprotein G-T (LOC139804), mRNA. |
| NM_004583 | SFRS10 | NP_004584 | Homo sapiens splicing factor, arginine/serine-rich 10 (transformer 2 homolog, Drosophila) (SFRS10), mRNA. |
| AL117507 | DKFZp434F19.35 | CAB55969 | Homo sapiens mRNA; cDNA DKFZp434F1935 (from clone DKFZp434F1935); partial cds. |

Figure 16 (2)

| Gene Symbol | | Nucleotide Sequence Description | |
|----------------------------|-------------------------------|---|--|
| GenBank Accession for mRNA | GenBank Accession for Protein | | |
| AB020657 | KIAA0850 | Homo sapiens mRNA for KIAA0850 protein, partial cds. | |
| AB033019 | KIAA1193 | Homo sapiens mRNA for KIAA1193 protein, partial cds. | |
| AF026564 | RBMI | Homo sapiens RNA binding protein II (RBMI) gene, complete cds. | |
| AF165518 | MAGOH | Homo sapiens MAGOH isoform (MAGOH) mRNA, complete cds. | |
| AF273304 | | Homo sapiens XPMC2 protein mRNA, complete cds. | |
| AL117507 | DKFZp434F193 | Homo sapiens mRNA; cDNA DKFZp434F1935 (from clone DKFZp434F1935); partial cds. | |
| L01457 | | | |
| NM_000455 | STK11 | Homo sapiens (clone JH4B1) PM-scl autoantigen mRNA, complete cds. | |
| NM_000982 | RPL21 | Homo sapiens serine/threonine kinase 11 (Peutz-Jeghers syndrome) (STK11), mRNA. | |
| NM_000996 | RPL35A | Homo sapiens ribosomal protein L21 (RPL21), mRNA. | |
| NM_000999 | RPL38 | Homo sapiens ribosomal protein L35a (RPL35A), mRNA. | |
| NM_001004 | RPLP2 | Homo sapiens ribosomal protein L38 (RPL38), mRNA. | |
| NM_001011 | RPS7 | Homo sapiens ribosomal protein; large P2 (RPLP2), mRNA. | |
| NM_001026 | RPS24 | Homo sapiens ribosomal protein S7 (RPS7), mRNA. | |
| NM_001032 | RPS29 | Homo sapiens ribosomal protein S24 (RPS24), transcript variant 2, mRNA. | |
| NM_001112 | ADARB1 | Homo sapiens ribosomal protein S29 (RPS29), mRNA. | |
| NM_001356 | DDX3X | Homo sapiens adenosine deaminase, RNA-specific, B1 (RED1 homolog rat) (ADARB1), transcript variant DRADA2a, mRNA. | |
| NM_001357 | DHX9 | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, X-linked (DDX3X), transcript variant 2, mRNA. | |
| NM_001618 | ADPRT | Homo sapiens DEAH (Asp-Glu-Ala-His) box polypeptide 9 (DHX9), transcript variant 1, mRNA. | |
| NM_002520 | NPM1 | Homo sapiens ADP-ribosyltransferase (NAD ⁺ ; poly (ADP-ribose) polymerase) (ADPRT), mRNA. | |
| NM_002967 | SAFB | Homo sapiens nucleophosmin (nucleolar phosphoprotein B23, numatrin) (NPM1), mRNA. | |
| NM_003133 | SRP9 | Homo sapiens scaffold attachment factor B (SAFB), mRNA. | |
| NM_003429 | ZNF85 | Homo sapiens signal recognition particle 9kDa (SRP9), mRNA. | |
| NM_003472 | DEK | Homo sapiens zinc finger protein 85 (HPF4, HTF1) (ZNF85), mRNA. | |
| NM_003675 | PRPF18 | Homo sapiens DEK oncogene (DNA binding) (DEK), mRNA. | |
| NM_003895 | SYNJ1 | Homo sapiens PRP18 pre-mRNA processing factor 18 homolog (yeast) (PRPF18), mRNA. | |
| NM_004169 | SHMT1 | Homo sapiens synaptotagmin 1 (SYNJ1), transcript variant 1, mRNA. | |
| NM_004289 | NFE2L3 | Homo sapiens serine hydroxymethyltransferase 1 (soluble) (SHMT1), transcript variant 1, mRNA. | |
| NM_004396 | DDX5 | Homo sapiens nuclear factor (erythroid-derived 2)-like 3 (NFE2L3), mRNA. | |
| NM_004990 | MARS | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 5 (DDX5), mRNA. | |
| NM_005083 | U2AF1L1 | Homo sapiens methionine-tRNA synthetase (MARS), mRNA. | |
| NM_005548 | KARS | Homo sapiens U2(RNU2) small nuclear RNA auxiliary factor 1-like 1 (U2AF1L1), mRNA. | |
| NM_006624 | BS69 | Homo sapiens lysyl-tRNA synthetase (KARS), mRNA. | |
| | | Homo sapiens adenovirus 5 E1A binding protein (BS69), mRNA. | |

Figure 17 (11)

| Gene Symbol | | Nucleotide Sequence Description | |
|----------------------------|-------------------------------|--|--|
| GenBank Accession for mRNA | GenBank Accession for Protein | | |
| NM_007020 | U1SNRNPBP | Homo sapiens U1-snRNP binding protein homolog (U1SNRNPBP), transcript variant 1, mRNA. | |
| NM_007080 | LSM6 | Homo sapiens LSM6 homolog, U6 small nuclear RNA associated (S. cerevisiae) (LSM6), mRNA. | |
| NM_007362 | NCBP2 | Homo sapiens nuclear cap binding protein subunit 2, 20kDa (NCBP2), mRNA. | |
| NM_012255 | XRN2 | Homo sapiens 5'-3' exoribonuclease 2 (XRN2), mRNA. | |
| NM_012423 | RPL13A | Homo sapiens ribosomal protein L13a (RPL13A), mRNA. | |
| NM_014977 | ACINUS | Homo sapiens apoptotic chromatin condensation inducer in the nucleus (ACINUS), mRNA. | |
| NM_015934 | NOP5/NOP58 | Homo sapiens nucleolar protein NOP5/NOP58 (NOP5/NOP58), mRNA. | |
| NM_016480 | PAIP2 | Homo sapiens poly(A) binding protein interacting protein 2 (PAIP2), mRNA. | |
| NM_017840 | MRPL16 | Homo sapiens mitochondrial ribosomal protein L16 (MRPL16), nuclear gene encoding mitochondrial protein, mRNA. | |
| NM_018281 | FLJ10948 | Homo sapiens hypothetical protein FLJ10948 (FLJ10948), mRNA. | |
| NM_018427 | RRN3 | Homo sapiens RNA polymerase I transcription factor RRN3 (RRN3), mRNA. | |
| NM_018664 | SNFT | Homo sapiens Jun dimerization protein p21SNFT (SNFT), mRNA. | |
| NM_021104 | RPL41 | Homo sapiens ribosomal protein L41 (RPL41), mRNA. | |
| _022551 | RPS18 | Homo sapiens ribosomal protein S18 (RPS18), mRNA. | |
| _031210 | DC50 | Homo sapiens hypothetical protein DC50 (DC50), mRNA. | |
| _001524 | LOC151173 | Homo sapiens similar to TAR DNA-binding protein-43 (TDP-43) (LOC151173), mRNA. | |
| _016729 | LOC157679 | Homo sapiens similar to nuclear receptor coactivator 6 interacting protein (H. sapiens) (LOC157679), mRNA. | |
| _031058 | LOC147647 | Homo sapiens similar to nucleolar protein interacting with the FHA domain of pKi-67 (H. sapiens) (LOC147647), mRNA. | |
| _047920 | LOC92906 | Homo sapiens similar to Unknown (protein for IMAGE:3587716) (LOC92906), mRNA. | |
| _058430 | LOC119880 | Homo sapiens similar to hypothetical protein similar to RNA-binding protein lark (LOC119880), mRNA. | |
| _058943 | LOC125925 | Homo sapiens similar to R32611_1 (LOC125925), mRNA. | |
| XM_059194 | LOC127933 | Homo sapiens hypothetical protein BC014917 (LOC127933), mRNA. | |
| XM_059936 | LOC138046 | Homo sapiens similar to RNA-binding protein Raly (LOC138046), mRNA. | |
| XM_060808 | LOC128072 | Homo sapiens similar to Vigilin (High density lipoprotein-binding protein) (HDL-binding protein) (LOC128072), mRNA. | |
| XM_067452 | LOC131596 | Homo sapiens similar to splicing factor 3a, subunit 2, 66kD; Spliceosome protein SAP-62 (LOC131596), mRNA. | |
| XM_068248 | LOC133225 | Homo sapiens similar to heterogeneous ribonuclear particle protein A1.beta - human (LOC133225), mRNA. | |
| XM_068457 | LOC133655 | Homo sapiens similar to splicing coactivator subunit SRm300; RNA binding protein; AT-rich element binding factor; serine/arginine repetitive matrix 2 (LOC133655), mRNA. | |
| XM_088640 | LOC158685 | Homo sapiens similar to bA353C18.3.2 (splicing factor CC1.3, isoform 2 (CC1.4)) (LOC158685), mRNA. | |

Figure 17 (2)

| Gene Symbol | | Nucleotide Sequence Description | |
|----------------------------|-------------------------------|---|--|
| GenBank Accession for mRNA | GenBank Accession for Protein | | |
| XM_093336 NM_000971 | XP_093336 NP_000962 | mRNA. Homo sapiens similar to Eukaryotic translation initiation factor 4B (eIF-4B) (LOC165631), mRNA. Homo sapiens ribosomal protein L7 (RPL7), mRNA. | |

Figure 17(3)

| GenBank Accession for mRNA | Gene Symbol | GenBank Accession for Protein | Nucleotide Sequence Description |
|----------------------------------|----------------|-------------------------------------|--|
| XM_091042 | LOC16168 | XP_091042 | Homo sapiens similar to data source:MGD, source key:MGI:107795, evidence:ISS-heterogeneous |
| XM_068433 | LOC13361 | XP_068433 | nuclear ribonucleoprotein C-putative (LOC161682), mRNA. |
| XM_093259 | LOC17033 | XP_093259 | Homo sapiens similar to Putative RNA-binding protein 15 (RNA binding motif protein 15) (One-twenty two protein) (LOC133616), mRNA. |
| XM_085059 | LOC14522 | XP_085059 | Homo sapiens similar to RBM1 (LOC170330), mRNA. |
| AF121255 | EIF2C2 | AAF13034 | Homo sapiens similar to Splicing factor 3B subunit 4 (Spliceosome associated protein 49) (SAP 49) (SF3b50) (Pre-mRNA splicing factor SF3b 49 kDa subunit) (LOC145223), mRNA. |
| NM_005664 | MKRN3 | NP_005655 | Homo sapiens protein translation initiation factor 2C2 (EIF2C2) mRNA, partial cds. |
| NM_001357 | DHX8 | NP_001348 | Homo sapiens makorin, ring finger protein, 3 (MKRN3), mRNA. |
| NM_030941 | LOC81691 | NP_112203 | Homo sapiens DEAH (Asp-Glu-Ala-His) box polypeptide 9 (DHX9), transcript variant 1, mRNA. |
| NM_014852 | KIAA0682 | NP_055667 | Homo sapiens exonuclease NEF-sp (LOC81691), mRNA. |
| NM_000246 | MHC2TA | NP_000237 | Homo sapiens KIAA0682 gene product (KIAA0682), mRNA. |
| JM_007165 | SF3A2 | NP_009096 | Homo sapiens MHC class II transactivator (MHC2TA), mRNA. |
| JM_005384 | NFIL3 | NP_005375 | Homo sapiens splicing factor 3a, subunit 2, 66kDa (SF3A2), mRNA. |
| JM_018427 | RRN3 | NP_060897 | Homo sapiens nuclear factor, interleukin 3 regulated (NFIL3), mRNA. |
| CM_060212 | LOC12686 | XP_060212 | Homo sapiens RNA polymerase I transcription factor RRN3 (RRN3), mRNA. |
| JM_004895 | CIAS1 | NP_004886 | Homo sapiens similar to tudor repeat associator with PCTAIRE 2 (LOC126861), mRNA. |
| JM_003760 | EIF3S10 | NP_003741 | Homo sapiens cold autoinflammatory syndrome 1 (CIAS1), transcript variant 1, mRNA. |
| CM_092386 | LOC16511 | XP_092386 | Homo sapiens eukaryotic translation initiation factor 3, subunit 10 theta, 150/170kDa (EIF3S10), mRNA. |
| JM_007294 | BRCA1 | NP_009225 | Homo sapiens similar to KIAA1841 protein (LOC165115), mRNA. |
| NM_001991 | EZH1 | NP_001982 | Homo sapiens breast cancer 1, early onset (BRCA1), transcript variant BRCA1a, mRNA. |
| XM_010852 | LOC15124 | XP_010852 | Homo sapiens enhancer of zeste homolog 1 (Drosophila) (EZH1), mRNA. |
| NM_002502 | NFKB2 | NP_002493 | Homo sapiens similar to helix-destabilizing protein - rat (LOC151249), mRNA. |
| NM_000946 | PRIM1 | NP_000937 | Homo sapiens nuclear factor of kappa light polypeptide gene enhancer in B-cells 2 (p49/p100) (NFKB2), mRNA. |
| NM_006893 | LGTM | NP_006824 | Homo sapiens primase, polypeptide 1, 49kDa (PRIM1), mRNA. |
| XM_094140 | LOC16686 | XP_094140 | Homo sapiens ligatin (LGTM), mRNA. |
| AF083441 | LOC13365 | AAD52028 | Homo sapiens similar to Apobec-1 complementation factor, APOBEC-1 stimulating protein (LOC166863), mRNA. |
| XM_068457 | LOC13365 | XP_068457 | Homo sapiens SU11 Isolog mRNA, complete cds. |
| | | | Homo sapiens similar to splicing coactivator subunit SRm300; RNA binding protein; AT-rich element binding factor; serine/arginine repetitive matrix 2 (LOC133655), mRNA. |

Figure 18 (1)

| GenBank Accession for mRNA | Gene Symbol | GenBank Accession for Protein | Nucleotide Sequence Description |
|----------------------------------|----------------|-------------------------------------|---|
| NM_000125 | ESR1 | NP_000116 | Homo sapiens estrogen receptor 1 (ESR1), mRNA. |
| NM_015971 | MRPS7 | NP_057055 | Homo sapiens mitochondrial ribosomal protein S7 (MRPS7), nuclear gene encoding mitochondrial protein, mRNA. |
| NM_032514 | MAP1LC3 A | NP_115903 | Homo sapiens microtubule-associated protein 1 light chain 3 alpha (MAP1LC3A), transcript variant 1, mRNA. |
| NM_004504 | HRB | NP_004495 | Homo sapiens HIV-1 Rev binding protein (HRB), mRNA. |
| NM_001029 | RPS26 | NP_001020 | Homo sapiens ribosomal protein S26 (RPS26), mRNA. |
| NM_002535 | OAS2 | NP_002526 | Homo sapiens 2'-5'-oligoadenylate synthetase 2, 69/71kDa (OAS2), transcript variant 2, mRNA. |
| NM_003325 | HIRA | NP_003316 | Homo sapiens HIR histone cell cycle regulation defective homolog A (S. cerevisiae) (HIRA), mRNA. |

Figure 18(2)

| GenBank Accession for mRNA | Gene Symbol | GenBank Accession for Protein | Nucleotide Sequence Description |
|----------------------------------|----------------|-------------------------------------|--|
| NM_092652 | LOC165534 | XP_092652 | Homo sapiens LOC165534 (LOC165534), mRNA. |
| NM_004705 | PRKRIR | NP_004696 | Homo sapiens protein-kinase, interferon-inducible double stranded RNA dependent inhibitor, repressor of (P58 repressor) (PRKRIR), mRNA. |
| NM_001537 | HSBP1 | NP_001528 | Homo sapiens heat shock factor binding protein 1 (HSBP1), mRNA. |
| XM_070624 | LOC137819 | XP_070624 | Homo sapiens LOC137819 (LOC137819), mRNA. |
| NM_006397 | RNASEH2A | NP_006388 | Homo sapiens RNASEH2A, mRNA. |
| NM_012423 | RPL13A | NP_036555 | Homo sapiens ribosomal protein L13a (RPL13A), mRNA. |
| XM_085059 | LOC145223 | XP_085059 | Homo sapiens similar to Splicing factor 3B subunit 4 (Spliceosome associated protein 49) (SAP 49) (SF3b50) (Pre-mRNA splicing factor SF3b 49 kDa subunit) (LOC145223), mRNA. |
| NM_003136 | SRP54 | NP_003127 | Homo sapiens signal recognition particle 54kDa (SRP54), mRNA. |
| XM_091653 | LOC162582 | XP_091653 | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 (HELIX-DESTABILIZING PROTEIN) (SINGLE-STRAND BINDING PROTEIN) (HNRNP CORE PROTEIN A1) (LOC162582), mRNA. |
| NM_005657 | TP53BP1 | NP_005648 | Homo sapiens tumor protein p53 binding protein, 1 (TP53BP1), mRNA. |
| M_004491 | GRLF1 | NP_004482 | Homo sapiens glucocorticoid receptor DNA binding factor 1 (GRLF1), transcript variant 2, mRNA. |
| M_007205 | TREX2 | NP_009136 | Homo sapiens three prime repair exonuclease 2 (TREX2), transcript variant 1, mRNA. |
| M_006565 | CTCF | NP_008556 | Homo sapiens CCCTC-binding factor (zinc finger protein) (CTCF), mRNA. |
| AF026563 | RBML1 | | Homo sapiens RBML1 gene, exon 6. |
| M_007297 | BRCA1 | NP_009228 | Homo sapiens breast cancer 1, early onset (BRCA1), transcript variant BRCA1-delta2-10, mRNA. |
| M_004569 | NSEP1 | NP_004550 | Homo sapiens nuclease sensitive element binding protein 1 (NSEP1), mRNA. |
| M_060358 | LOC127164 | XP_060358 | Homo sapiens similar to TAR DNA binding protein (LOC127164), mRNA. |
| M_003685 | KHSRP | NP_003678 | Homo sapiens KH-type splicing regulatory protein (FUSE binding protein 2) (KHSRP), mRNA. |
| M_005115 | MVP | NP_005106 | Homo sapiens major vault protein (MVP), transcript variant 2, mRNA. |
| M_002904 | RDBP | NP_002895 | Homo sapiens RD RNA binding protein (RDBP), mRNA. |
| M_005772 | RCL1 | NP_005763 | Homo sapiens RNA terminal phosphate cyclase-like 1 (RCL1), mRNA. |
| X88494 | mpp10 | CAA67120 | H.sapiens mRNA for M phase phosphoprotein 10. |
| NM_015062 | PPRC1 | NP_055877 | Homo sapiens peroxisome proliferative activated receptor, gamma, coactivator-related 1 (PPRC1), mRNA. |
| AF083441 | | AAD52028 | Homo sapiens SUI1 Isolog mRNA, complete cds. |
| XM_068457 | LOC133655 | XP_068457 | Homo sapiens similar to splicing coactivator subunit SRM300; RNA binding protein; AT-rich element binding factor, serine/arginine repetitive matrix 2 (LOC133655), mRNA. |
| AK000256 | | BAA91036 | Homo sapiens cDNA FLJ20249 fis, clone COLF6621. |
| NM_004599 | SREBF2 | NP_004590 | Homo sapiens sterol regulatory element binding transcription factor 2 (SREBF2), mRNA. |
| NM_005968 | HNRPM | NP_005959 | Homo sapiens heterogeneous nuclear ribonucleoprotein M (HNRPM), transcript variant 1, mRNA. |
| BC000138 | HNRPM | AAH00138 | Homo sapiens heterogeneous nuclear ribonucleoprotein M, transcript variant 1, mRNA (cDNA clone MGC:5136 IMAGE:2900532), complete cds. |

Figure 19 (1)

| Gene Accession | Gene Symbol | GenBank Accession for Protein | Nucleotide Sequence Description |
|-------------------|----------------|-------------------------------------|--|
| NM_004992 | MECP2 | NP_004983 | Homo sapiens methyl CpG binding protein 2 (Rett syndrome) (MECP2), mRNA. |
| NM_001714 | BICD1 | NP_001705 | Homo sapiens Bicaudal D homolog 1 (Drosophila) (BICD1), mRNA. |
| NM_015409 | EP400 | NP_056224 | Homo sapiens E1A binding protein p400 (EP400), mRNA. |
| BC007052 | HNRPC | AAH07052 | Homo sapiens heterogeneous nuclear ribonucleoprotein C (C1/C2), mRNA (cDNA clone MGC:12469 IMAGE:3686841), complete cds. |
| NM_012426 | SF3B3 | NP_036558 | Homo sapiens splicing factor 3b, subunit 3, 130kDa (SF3B3), mRNA. |
| NM_003016 | SFRS2 | NP_003007 | Homo sapiens splicing factor, arginine/serine-rich 2 (SFRS2), mRNA. |
| NM_002694 | POLR2C | NP_002685 | Homo sapiens polymerase (RNA) II (DNA directed) polypeptide C, 33kDa (POLR2C), transcript variant alpha, mRNA. |
| NM_002197 | ACO1 | NP_002188 | Homo sapiens aconitase 1, soluble (ACO1), mRNA. |
| AF075000 | H_YH95C04.1 | AAC28457 | Homo sapiens full length insert cDNA YH95C04. |
| BC002395 | SF3A3 | AAH02395 | Homo sapiens splicing factor 3a, subunit 3, 60kDa, mRNA (cDNA clone MGC:8445 IMAGE:2821350), complete cds. |
| U056568 | LOC147774 | XP_056568 | Homo sapiens similar to KH-type splicing regulatory protein (FUSE binding protein 2) (H. sapiens) (LOC147774), mRNA. |
| U004846 | EIF4EL3 | NP_004837 | Homo sapiens eukaryotic translation initiation factor 4E-like 3 (EIF4EL3), mRNA. |
| U005463 | HNRPDL | NP_005454 | Homo sapiens heterogeneous nuclear ribonucleoprotein D-like (HNRPDL), transcript variant 1, mRNA. |
| U067844 | LOC132430 | XP_067844 | Homo sapiens similar to Polyadenylate-binding protein 4 (Poly(A)-binding protein 4) (PABP 4) (Inducible poly(A)-binding protein) (iPABP) (Activated-platelet protein-1) (APP-1) (LOC132430), mRNA. |
| U006112 | PPIE | NP_006103 | Homo sapiens peptidylprolyl isomerase E (cyclophilin E) (PPIE), transcript variant 1, mRNA. |
| U017840 | MRPL16 | NP_060310 | Homo sapiens mitochondrial ribosomal protein L16 (MRPL16), nuclear gene encoding mitochondrial protein, mRNA. |
| U030621 | DICER1 | NP_085124 | Homo sapiens Dicer1, Dcr-1 homolog (Drosophila) (DICER1), transcript variant 2, mRNA. |
| U004397 | DDX6 | NP_004388 | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 6 (DDX6), mRNA. |
| NM_002111 | HD | NP_002102 | Homo sapiens huntingtin (Huntington disease) (HD), mRNA. |
| AL021546 | SFRS9 | CAA16498 | Human DNA sequence from clone XX-15E1 on chromosome 12, complete sequence. |
| NM_033501 | TRERF1 | NP_277036 | Homo sapiens transcriptional regulating factor 1 (TRERF1), transcript variant 2, mRNA. |
| BC012090 | | AAH12090 | Homo sapiens, Similar to heterogeneous nuclear ribonucleoprotein A3, clone MGC:20045 IMAGE:4661041, mRNA, complete cds. |
| NM_006546 | IMP-1 | NP_006537 | Homo sapiens IGF-1I mRNA-binding protein 1 (IMP-1), mRNA. |
| XM_068928 | LOC134611 | XP_068928 | Homo sapiens similar to TAR DNA binding protein (LOC134611), mRNA. |
| NM_016381 | TREX1 | NP_057465 | Homo sapiens three prime repair exonuclease 1 (TREX1), transcript variant 1, mRNA. |
| NM_017518 | TREX2 | NP_059988 | Homo sapiens three prime repair exonuclease 2 (TREX2), transcript variant 5, mRNA. |
| NM_015646 | RAP1B | NP_056461 | Homo sapiens RAP1B, member of RAS oncogene family (RAP1B), mRNA. |
| NM_052840 | BRUNOL6 | NP_443072 | Homo sapiens bruno-like 6, RNA binding protein (Drosophila) (BRUNOL6), mRNA. |

Figure 19(2)

| GenBank Accession for mRNA | Gene Symbol | GenBank Accession for Protein | Nucleotide Sequence Description |
|----------------------------|-------------|-------------------------------|--|
| NM_001538 | HSF4 | NP_001528 | 1' to sapiens heat shock transcription factor 4 (HSF4), mRNA. |
| XM_063246 | LOC122663 | XP_063246 | ...omo sapiens LOC122663 (LOC122663), mRNA. |
| XM_063244 | LOC122661 | XP_063244 | Homo sapiens similar to Nonsecretory ribonuclease precursor (Ribonuclease US) (Eosinophil-derived neurotoxin) (RNase Upl-2) (Ribonuclease 2) (RNase 2) (LOC122661), mRNA. |
| AW607076 | | | PM0-HT0452-140100-002-e07 HT0452 Homo sapiens cDNA, mRNA sequence. |
| NM_016816 | OAS1 | NP_058132 | Homo sapiens 2',5'-oligoadenylate synthetase 1, 40/46kDa (OAS1), transcript variant E18, mRNA. |
| NM_004175 | SNRPD3 | NP_004166 | Homo sapiens small nuclear ribonucleoprotein D3 polypeptide 18kDa (SNRPD3), mRNA. |
| AB020657 | KIAA0850 | BAA74873 | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 17, mRNA (cDNA clone MGC:2030 IMAGE:3345982), complete cds. |
| BC000595 | DDX17 | AAH00595 | Homo sapiens similar to splicing factor 3a, subunit 2, 66kD; Spliceosome protein SAP-62 (LOC152994), mRNA. |
| XM_094158 | LOC152994 | XP_094158 | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 20 (DDX20), mRNA. |
| NM_007204 | DDX20 | NP_009135 | Homo sapiens transcription termination factor, mitochondrial (MTERF), nuclear gene encoding mitochondrial protein, mRNA. |
| NM_006980 | MTERF | NP_008911 | Homo sapiens neuro-oncological ventral antigen 1 (NOVA1), transcript variant 3, mRNA. |
| U_006491 | NOVA1 | NP_006482 | Homo sapiens Splicing factor, arginine/serine-rich, 46kD (SRP46), mRNA. |
| U_032102 | SRP46 | NP_115285 | Homo sapiens MAGOH mRNA, complete cds. |
| F035940 | MAGOH | AAC39606 | Homo sapiens similar to hypothetical protein BC011593 (LOC139891), mRNA. |
| U_066948 | LOC139891 | XP_066948 | Homo sapiens splicing factor 3a, subunit 2, 66kDa (SF3A2), mRNA. |
| U_007165 | SF3A2 | NP_009096 | Homo sapiens nuclear transcription factor Y, gamma (NFYC), mRNA. |
| U_014223 | NFYC | NP_055038 | Homo sapiens similar to Heterogeneous nuclear ribonucleoprotein A3 homolog 2 (hnRNP A3(B)) (LOC170270), mRNA. |
| U_093219 | LOC170270 | XP_093219 | Homo sapiens heterogeneous nuclear ribonucleoprotein A2/B1 (HNRPA2B1), transcript variant A2, mRNA. |
| U_002137 | HNRPA2B1 | NP_002128 | Homo sapiens mRNA for TRABID protein (TRABID gene). |
| U_252060 | TRABID | CAB64449 | Homo sapiens apoptotic chromatin condensation inducer in the nucleus (ACINUS), mRNA. |
| NM_014977 | ACINUS | NP_055792 | Homo sapiens similar to RIKEN cDNA C130020J04 (LOC167540), mRNA. |
| XM_094555 | LOC167540 | XP_094555 | Homo sapiens similar to Heterogeneous nuclear ribonucleoprotein A1 (Helix-destabilizing protein) (Single-strand binding protein) (hnRNP core protein A1) (HDP-1) (Topoisomerase-inhibitor suppressed) (LOC130800), mRNA. |
| XM_065946 | LOC130800 | XP_065946 | Homo sapiens breast and ovarian cancer susceptibility protein splice variant (BRCA1) mRNA, complete cds. |
| AF005068 | BRCA1 | AAB61673 | Homo sapiens chromosome 20 open reading frame 14 (C20orf14), mRNA. |
| NM_012469 | C20orf14 | NP_036601 | Homo sapiens poly(A) binding protein, nuclear 1 (PABPN1), mRNA. |
| NM_004643 | PABPN1 | NP_004634 | Homo sapiens HIR histone cell cycle regulation defective homolog A (S. cerevisiae) (HIRA), mRNA. |
| NM_003325 | HIRA | NP_003316 | |

Figure 1a(3)

| GenBank Accession for mRNA | Gene Symbol | GenBank Accession for Protein | Nucleotide Sequence Description |
|----------------------------------|----------------|-------------------------------------|--|
| NM_019038 | TDRD4 | NP_061911 | Homo sapiens tudor domain containing 4 (TDRD4), mRNA. |
| NM_025065 | RPF1 | NP_079341 | Homo sapiens RNA processing factor 1 (RPF1), mRNA. |
| NM_005877 | SF3A1 | NP_005868 | Homo sapiens splicing factor 3a, subunit 1, 120kDa (SF3A1), mRNA. |
| NM_002138 | HNRPD | NP_002129 | Homo sapiens heterogeneous nuclear ribonucleoprotein D (AU-rich element RNA binding protein 1, 37kDa) (HNRPD), transcript variant 3, mRNA. |
| XM_058876 | MGC49942 | XP_058876 | Homo sapiens hypothetical protein MGC49942 (MGC49942), mRNA. |
| NM_021976 | RXRB | NP_068811 | Homo sapiens retinoid X receptor, beta (RXRB), mRNA. |
| NM_003489 | NRIP1 | NP_003480 | Homo sapiens nuclear receptor interacting protein 1 (NRIP1), mRNA. |
| M29916 | RMRP | | Human mitochondrial RNA-processing endoribonuclease RNA (mrp) gene; complete cds. |
| XM_066446 | LOC139051 | XP_066446 | Homo sapiens similar to pol protein (LOC139051), mRNA. |

Figure 19(4)

| GenBank Accession for mRNA | Gene Symbol | GenBank Accession for Protein | Nucleotide Sequence Description |
|----------------------------|-------------|-------------------------------|--|
| NM_007297 | BRCA1 | NP_009228 | Homo sapiens breast cancer 1, early onset (BRCA1), transcript variant BRCA1-delta2-10, mRNA. |
| NM_022830 | FLJ22347 | NP_073741 | Homo sapiens hypothetical protein FLJ22347 (FLJ22347), mRNA. |
| NM_018722 | HSA0461 | NP_061192 | Homo sapiens BWRP protein (HSA04617), mRNA. |
| XM_058876 | MGC49942 | XP_058876 | Homo sapiens hypothetical protein MGC49942 (MGC49942), mRNA. |
| NM_015698 | T54 | NP_056513 | Homo sapiens T54 protein (T54), mRNA. |
| XM_050102 | LOC12663 | XP_060102 | Homo sapiens LOC126635 (LOC126635), mRNA. |
| NM_013316 | CNOT4 | NP_037448 | Homo sapiens CCR4-NOT transcription complex, subunit 4 (CNOT4), mRNA. |
| AB033019 | KIAA1193 | BAA86507 | Homo sapiens mRNA for KIAA1193 protein, partial cds. |
| XM_067598 | LOC13189 | XP_067598 | Homo sapiens similar to POLYADENYLATE-BINDING PROTEIN 2 (POLY(A) BINDING PROTEIN 2) (PABP 2) (LOC131898), mRNA. |
| NM_000937 | POLR2A | NP_000928 | Homo sapiens polymerase (RNA) II (DNA directed) polypeptide A, 220kDa (POLR2A), mRNA. |
| XM_087530 | LOC15282 | XP_087530 | Homo sapiens similar to hypothetical protein FLJ20273 (LOC152827), mRNA. |
| V_047272 | LOC92781 | XP_047272 | Homo sapiens similar to dJ309K20.4 (KIAA0765, putative brain nuclear targeted protein (HRIHFB2091, RNA recognition motif (RNP, RRM or RBD domain) containing protein)) (LOC92781), mRNA. |
| V_090177 | LOC16025 | XP_090177 | Homo sapiens similar to nuclear matrix protein NMP200 related to splicing factor PRP19 (H. sapiens) (LOC160258), mRNA. |
| J252060 | TRABID | CAB64449 | Homo sapiens mRNA for TRABID protein (TRABID gene). |
| V_007185 | TNRC4 | NP_009116 | Homo sapiens trinucleotide repeat containing 4 (TNRC4), mRNA. |
| B036532 | p53R2 | BAA92493 | Homo sapiens p53R2 gene for ribonucleotide reductase, exon 9 and complete cds. |
| V_005119 | THRAP3 | NP_005110 | Homo sapiens thyroid hormone receptor associated protein 3 (THRAP3), mRNA. |
| V_013235 | RNASE3L | NP_037367 | Homo sapiens nuclear RNase III Drosha (RNASE3L), mRNA. |
| V_004175 | SNRPD3 | NP_004168 | Homo sapiens small nuclear ribonucleoprotein D3 polypeptide 18kDa (SNRPD3), mRNA. |
| XM_066586 | LOC13926 | XP_066586 | Homo sapiens similar to Con1 (LOC139264), mRNA. |
| NM_018122 | FLJ10514 | NP_060592 | Homo sapiens hypothetical protein FLJ10514 (FLJ10514), mRNA. |
| NM_006540 | NCOA2 | NP_006531 | Homo sapiens nuclear receptor coactivator 2 (NCOA2), mRNA. |
| BC004154 | NR2F1 | AAH04154 | Homo sapiens nuclear receptor subfamily 2, group F, member 1, mRNA (cDNA clone MGC:2388 IMAGE:2824138), complete cds. |
| NM_006567 | FARS1 | NP_006558 | Homo sapiens phenylalanine-tRNA synthetase 1 (mitochondrial) (FARS1), nuclear gene encoding mitochondrial protein, mRNA. |
| XM_086782 | LOC15015 | XP_086792 | Homo sapiens similar to SPlicing FACTOR U2AF 35 KD SUBUNIT (U2 AUXILIARY FACTOR 35 KD SUBUNIT) (U2 SNRNP AUXILIARY FACTOR SMALL SUBUNIT) (LOC150152), mRNA. |
| AF084974 | EXO1 | AAD13754 | Homo sapiens exonuclease I (EXO1) mRNA, complete cds. |

Figure 20 (1)

| GenBank Accession for mRNA | Gene Symbol | GenBank Accession for Protein | Nucleotide Sequence Description |
|----------------------------------|----------------|-------------------------------------|--|
| XM_064113 | LOC12438 | XP_064113 | Homo sapiens LOC124380 (LOC124380), mRNA. |
| NM_002904 | RDBP | NP_002895 | Homo sapiens RD RNA binding protein (RDBP), mRNA. |
| NM_005463 | HNRPD | NP_005454 | Homo sapiens heterogeneous nuclear ribonucleoprotein D-like (HNRPD), transcript variant 1, mRNA. |
| NM_003244 | TGIF | NP_003235 | Homo sapiens TGFB-induced factor (TALE family homeobox) (TGIF), transcript variant 4, mRNA. |
| XM_070603 | LOC13778 | XP_070603 | Homo sapiens similar to ANTIGEN GOR (LOC137784), mRNA. |
| NM_018415 | TRERF1 | NP_060885 | Homo sapiens transcriptional regulating factor 1 (TRERF1), transcript variant 3, mRNA. |
| XM_065361 | LOC12971 | XP_065361 | Homo sapiens similar to tudor protein (LOC129715), mRNA. |
| NM_020158 | RRP46 | NP_064543 | Homo sapiens exosome component Rrp46 (RRP46), mRNA. |
| NM_004343 | CALR | NP_004334 | Homo sapiens calreticulin (CALR), mRNA. |
| NM_006112 | PPIE | NP_006103 | Homo sapiens peptidylprolyl isomerase E (cyclophilin E) (PPIE), transcript variant 1, mRNA. |
| NM_005877 | SF3A1 | NP_005868 | Homo sapiens splicing factor 3a, subunit 1, 120kDa (SF3A1), mRNA. |
| _001714 | BICD1 | NP_001705 | Homo sapiens Bicaudal D homolog 1 (Drosophila) (BICD1), mRNA. |
| _002467 | MYC | NP_002458 | Homo sapiens v-myc myelocytomatosis viral oncogene homolog (avian) (MYC), mRNA. |
| _014663 | JMJD2A | NP_055478 | Homo sapiens jumonji domain containing 2A (JMJD2A), mRNA. |
| _001436 | FBL | NP_001427 | Homo sapiens fibrillarin (FBL), mRNA. |
| _019038 | TDRD4 | NP_061911 | Homo sapiens tudor domain containing 4 (TDRD4), mRNA. |

Figure 20(2)

| GenBank | | Gene | | Nucleotide Sequence Description | |
|-----------|----------|----------|-----------------------|--|--|
| Accession | for mRNA | Symbol | Accession for Protein | | |
| NM_013302 | | EEF2K | NP_037434 | Homo sapiens elongation factor-2 kinase (EEF2K), mRNA. | |
| NM_017948 | | NOL8 | NP_060418 | Homo sapiens nucleolar protein 8 (NOL8), mRNA. | |
| XM_089332 | | LOC14938 | XP_089332 | Homo sapiens similar to ribosomal protein L22 protein; 60S ribosomal protein L22; Epstein-Barr-encoded RNA-associated protein; Epstein-Barr virus small RNA-associated protein; EBER-associated protein; heparin-binding protein 15; heparin-binding protein HBP15... (LOC149382), mRNA. | |
| AF001947 | | PRP3 | AAC09069 | Homo sapiens U4/U6-associated RNA splicing factor (PRP3) mRNA, complete cds. | |
| AF062105 | | IGH | AAC18141 | Homo sapiens clone 21u-19 immunoglobulin heavy chain variable region (IGH) mRNA, partial cds. | |
| NM_004169 | | SHMT1 | NP_004160 | Homo sapiens serine hydroxymethyltransferase 1 (soluble) (SHMT1), transcript variant 1, mRNA. | |
| NM_000982 | | RPL29 | NP_000983 | Homo sapiens ribosomal protein L29 (RPL29), mRNA. | |
| XM_060808 | | LOC12807 | XP_060808 | Homo sapiens similar to Vigilin (High density lipoprotein-binding protein) (HDL-binding protein) (LOC128072), mRNA. | |
| NM_003902 | | FUBP1 | NP_003893 | Homo sapiens far upstream element (FUSE) binding protein 1 (FUBP1), mRNA. | |
| XM_084392 | | LOC14296 | XP_084392 | Homo sapiens region containing tudor; Ras homolog enriched in brain 2 (LOC142966), mRNA. | |
| ^F391283 | | SSA1 | AAK76432 | Homo sapiens 11p15.5 clone LOH11A, partial sequence. | |
| A_003325 | | HIRA | NP_003316 | Homo sapiens HIR histone cell cycle regulation defective homolog A (S. cerevisiae) (HIRA), mRNA. | |
| A_070832 | | LOC13826 | XP_070832 | Homo sapiens similar to hypothetical protein (LOC138267), mRNA. | |
| A_088257 | | LOC15543 | XP_088257 | Homo sapiens hypothetical protein LOC155435 (LOC155435), mRNA. | |
| K021418 | | | | Homo sapiens cDNA FLJ11356 fis, clone HEMBA1000150, highly similar to Homo sapiens putative RNA helicase mRNA. | |
| J252060 | | TRABID | CAB64449 | Homo sapiens mRNA for TRABID protein (TRABID gene). | |
| A_014852 | | KIAA0682 | NP_055667 | Homo sapiens KIAA0682 gene product (KIAA0682), mRNA. | |
| A_005870 | | SAP18 | NP_005861 | Homo sapiens sin3-associated polypeptide, 18kDa (SAP18), mRNA. | |
| NM_005587 | | MEF2A | NP_005578 | Homo sapiens MADS box transcription enhancer factor 2, polypeptide A (myocyte enhancer factor 2A) (MEF2A), mRNA. | |
| NM_016169 | | SUFU | NP_057253 | Homo sapiens suppressor of fused homolog (Drosophila) (SUFU), mRNA. | |
| XM_089062 | | LOC14886 | XP_089062 | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 (HELIX-DESTABILIZING PROTEIN) (SINGLE-STRAND BINDING PROTEIN) (HNRNP CORE PROTEIN A1) (LOC148866), mRNA. | |
| NM_004875 | | POLR1C | NP_004866 | Homo sapiens polymerase (RNA) I polypeptide C, 30kDa (POLR1C), transcript variant 2, mRNA. | |
| AF129756 | | | AAD18092 | Homo sapiens MSH55 gene, partial cds; and CLIC1, DDAH, G6b, G6c, G5b, G6e, G6f, BAT5, G5b, CSK2B, BAT4, G4, Apo M, BAT3, BAT2, AIF-1, 1C7, LST-1, LTB, TNF, and LTA genes, complete cds. | |
| NM_014872 | | ZBTB5 | NP_055687 | Homo sapiens zinc finger and BTB domain containing 5 (ZBTB5), mRNA. | |

Figure 21(1)

| GenBank Accession for mRNA | Gene Symbol | GenBank Accession for Protein | Nucleotide Sequence Description |
|----------------------------|-------------|-------------------------------|---|
| NM_015629 | PRPF31 | NP_056444 | Homo sapiens PRP31 pre-mRNA processing factor 31 homolog (yeast) (PRPF31), mRNA. |
| NM_017921 | NPL4 | NP_060391 | Homo sapiens hypothetical protein FLJ20657 (NPL4), mRNA. |
| NM_002534 | OAS1 | NP_002525 | Homo sapiens 2',5'-oligoadenylate synthetase 1, 40/46kDa (OAS1), transcript variant E16, mRNA. |
| AF083441 | | AAD52028 | Homo sapiens SU11 isolog mRNA, complete cds. |
| AF026563 | RBM11 | | Homo sapiens RBM11 gene, exon 6. |
| NM_012330 | MYST4 | NP_038462 | Homo sapiens MYST histone acetyltransferase (monocytic leukemia) 4 (MYST4), mRNA. |
| NM_003298 | NR2C2 | NP_003289 | Homo sapiens nuclear receptor subfamily 2, group C, member 2 (NR2C2), mRNA. |
| XM_061319 | LOC11917 | XP_061319 | Homo sapiens similar to HETEROGENEOUS NUCLEAR RIBONUCLEOPROTEIN A1 (HELIX-DESTABILIZING PROTEIN) (SINGLE-STRAND BINDING PROTEIN) (HNRNP CORE PROTEIN A1) (LOC119177), mRNA. |
| XM_091974 | LOC14789 | XP_091974 | Homo sapiens similar to hypothetical protein DKFZp434l1930 (H. sapiens) (LOC147891), mRNA. |
| NM_032102 | SRP46 | NP_115285 | Homo sapiens Splicing factor, arginine/serine-rich, 46kD (SRP46), mRNA. |
| NM_052879 | LOC11325 | NP_443111 | Homo sapiens c-Mpl binding protein (LOC113251), transcript variant 1, mRNA. |
| A_019038 | TDRD4 | NP_061911 | Homo sapiens tudor domain containing 4 (TDRD4), mRNA. |
| A_000991 | RPL28 | NP_000982 | Homo sapiens ribosomal protein L28 (RPL28), mRNA. |
| A_006893 | LGTN | NP_008824 | Homo sapiens ligatin (LGTN), mRNA. |
| A_060102 | LOC12663 | XP_060102 | Homo sapiens LOC126635 (LOC126635), mRNA. |
| A_025065 | RPF1 | NP_079341 | Homo sapiens RNA processing factor 1 (RPF1), mRNA. |
| A_004774 | PPARBP | NP_004765 | Homo sapiens PPAR binding protein (PPARBP), mRNA. |
| A_022767 | FLJ12484 | NP_073604 | Homo sapiens hypothetical protein FLJ12484 (FLJ12484), mRNA. |
| A_007165 | SF3A2 | NP_009096 | Homo sapiens splicing factor 3a, subunit 2, 66kDa (SF3A2), mRNA. |
| A_068248 | LOC13322 | XP_068248 | Homo sapiens similar to heterogeneous ribonuclear particle protein A1.beta - human (LOC133225), mRNA. |
| NM_004039 | ANXA2 | NP_004030 | Homo sapiens annexin A2 (ANXA2), mRNA. |

Figure 21(2)

| Gene Symbol | | Nucleotide Sequence Description | |
|----------------------------|-------------------------------|---|--|
| GenBank Accession for mRNA | GenBank Accession for Protein | | |
| NM_007375 | NP_031401 | Homo sapiens TAR DNA binding protein (TARDBP), mRNA. | |
| NM_000978 | NP_000969 | Homo sapiens ribosomal protein L23 (RPL23), mRNA. | |
| NM_005035 | NP_005026 | Homo sapiens polymerase (RNA) mitochondrial (DNA directed) (POLRMT), nuclear gene encoding mitochondrial protein, mRNA. | |
| NM_018723 | NP_061193 | Homo sapiens ataxin 2-binding protein 1 (A2BP1), transcript variant 4, mRNA. | |
| NM_031274 | NP_112564 | Homo sapiens testis expressed sequence 13A (TEX13A), mRNA. | |
| NM_019037 | NP_061910 | Homo sapiens exosome complex exonuclease RRP41 (RRP41), mRNA. | |
| NM_002938 | NP_002929 | Homo sapiens ring finger protein 4 (RNF4), mRNA. | |
| NM_016024 | NP_057108 | Homo sapiens CGI-79 protein (CGI-79), mRNA. | |
| NM_000980 | NP_000971 | Homo sapiens ribosomal protein L18a (RPL18A), mRNA. | |
| NM_005842 | NP_005633 | Homo sapiens TAF7 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 55kDa (TAF7), mRNA. | |
| XM_094555 | XP_094555 | Homo sapiens similar to RIKEN cDNA C130020J04 (LOC167540), mRNA. | |
| NM_020967 | NP_066018 | Homo sapiens nuclear receptor coactivator 5 (NCOA5), mRNA. | |
| 006209 | NP_006200 | Homo sapiens ectonucleotide pyrophosphatase/phosphodiesterase 2 (autotaxin) (ENPP2), mRNA. | |
| 015934 | NP_057018 | Homo sapiens nucleolar protein NOP5/NOP58 (NOP5/NOP58), mRNA. | |
| 003170 | NP_003161 | Homo sapiens suppressor of Ty 6 homolog (S. cerevisiae) (SUTP6H), mRNA. | |
| 005772 | NP_005763 | Homo sapiens RNA terminal phosphate cyclase-like 1 (RCL1), mRNA. | |
| 063346 | XP_063346 | Homo sapiens similar to polypyrimidine-tract binding protein (LOC122888), mRNA. | |
| 026126 | AAC23476 | Homo sapiens heterogeneous nuclear ribonucleoprotein D (HNRPD) gene, complete cds. | |
| 000989 | NP_000980 | Homo sapiens ribosomal protein L30 (RPL30), mRNA. | |
| 267533 | AAF78955 | Homo sapiens CUG-binding protein LYLQ isoform mRNA, complete cds. | |
| 004491 | NP_004482 | Homo sapiens glucocorticoid receptor DNA binding factor 1 (GRLF1), transcript variant 2, mRNA. | |
| 005336 | NP_005327 | Homo sapiens high density lipoprotein binding protein (vigilin) (HDLBP), mRNA. | |
| 001870 | NP_001861 | Homo sapiens eukaryotic translation initiation factor 5A (EIF5A), mRNA. | |
| XM_062603 | XP_062603 | Homo sapiens similar to ITBA4 PROTEIN (H. sapiens) (LOC121372), mRNA. | |
| XM_001524 | XP_001524 | Homo sapiens region containing tudor; Ras homolog enriched in brain 2 (LOC142966), mRNA. | |
| XM_084392 | XP_084392 | Homo sapiens fuse-binding protein-interacting repressor (SIAHBP1), transcript variant 2, mRNA. | |
| NM_014281 | NP_055096 | Homo sapiens putative S1 RNA binding domain protein (PS1D), mRNA. | |
| NM_016505 | NP_057589 | Homo sapiens Sjogren syndrome antigen A2 (60kDa, ribonucleoprotein autoantigen SS-A/Ro) (SSA2), mRNA. | |
| NM_004600 | NP_004591 | Homo sapiens small nuclear ribonucleoprotein polypeptides B and B1 (SNRBP), transcript variant 2, mRNA. | |
| NM_003091 | NP_003082 | Homo sapiens tudor and KH domain containing (TDRKH), mRNA. | |
| NM_006862 | NP_006853 | Homo sapiens REST corepressor (RCOR), mRNA. | |
| NM_015156 | NP_055971 | | |

Figure 22 (1)

| Gene Symbol | | Nucleotide Sequence Description | |
|----------------------------|-------------------------------|---|--|
| GenBank Accession for mRNA | GenBank Accession for Protein | | |
| NM_018387 | STRBP | Homo sapiens spermatid perinuclear RNA binding protein (STRBP), mRNA. | |
| NM_003787 | NOL4 | Homo sapiens nucleolar protein 4 (NOL4), mRNA. | |
| NM_001356 | DDX3X | Homo sapiens DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, X-linked (DDX3X), transcript variant 2, mRNA. | |
| NM_012330 | MYST4 | Homo sapiens MYST histone acetyltransferase (monocytic leukemia) 4 (MYST4), mRNA. | |
| NM_007367 | RALY | Homo sapiens RNA binding protein (autoantigenic, hnRNP-associated with lethal yellow) (RALY), transcript variant 2, mRNA. | |
| NM_005548 | KARS | Homo sapiens lysyl-tRNA synthetase (KARS), mRNA. | |
| NM_001436 | FBL | Homo sapiens fibrillarin (FBL), mRNA. | |
| NM_012279 | JAZ | Homo sapiens double-stranded RNA-binding zinc finger protein JAZ (JAZ), mRNA. | |
| NM_002296 | LBR | Homo sapiens lamin B receptor (LBR), transcript variant 1, mRNA. | |
| NM_001071 | TYMS | Homo sapiens thymidylate synthetase (TYMS), mRNA. | |
| XM_062601 | LOC121365 | Homo sapiens similar to RBM1 (LOC121365), mRNA. | |
| NM_000982 | RPL21 | Homo sapiens ribosomal protein L21 (RPL21), mRNA. | |
| _058819 | MSI2 | Homo sapiens musashi homolog 2 (Drosophila) (MSI2), mRNA. | |
| _084825 | LOC143763 | Homo sapiens similar to coactivator activator (LOC143763), mRNA. | |
| _000971 | RPL7 | Homo sapiens ribosomal protein L7 (RPL7), mRNA. | |
| _049523 | HYPA | Homo sapiens huntingtin-interacting protein HYPA/FBP11 (HYPA) mRNA, partial cds. | |
| _000990 | RPL27A | Homo sapiens ribosomal protein L27a (RPL27A), mRNA. | |
| _001031 | RPS28 | Homo sapiens ribosomal protein S28 (RPS28), mRNA. | |
| _001021 | RPS17 | Homo sapiens ribosomal protein S17 (RPS17), mRNA. | |
| _017993 | FLJ10094 | Homo sapiens hypothetical protein FLJ10094 (FLJ10094), mRNA. | |
| _003651 | CSDA | Homo sapiens cold shock domain protein A (CSDA), mRNA. | |
| _001714 | BICD1 | Homo sapiens Bicaudal D homolog 1 (Drosophila) (BICD1), mRNA. | |
| _033360 | KRAS2 | Homo sapiens v-Ki-ras2 Kirsten rat sarcoma 2 viral oncogene homolog (KRAS2), transcript variant a, mRNA. | |
| L13848 | DDX9 | Human RNA helicase A mRNA, complete cds. | |
| BC004154 | NR2F1 | Homo sapiens nuclear receptor subfamily 2, group F, member 1, mRNA (cDNA clone MGC:2388 IMAGE:2824138), complete cds. | |
| NM_016304 | C15orf15 | Homo sapiens chromosome 15 open reading frame 15 (C15orf15), mRNA. | |
| NM_022551 | RPS18 | Homo sapiens ribosomal protein S18 (RPS18), mRNA. | |
| NM_003244 | TGIF | Homo sapiens TGFB-induced factor (TALE family homeobox) (TGIF), transcript variant 4, mRNA. | |
| NM_003095 | SNRPF | Homo sapiens small nuclear ribonucleoprotein polypeptide F (SNRPF), mRNA. | |
| NM_003017 | SFRS3 | Homo sapiens splicing factor, arginine/serine-rich 3 (SFRS3), mRNA. | |
| NM_033246 | PML | Homo sapiens promyelocytic leukemia (PML), transcript variant 7, mRNA. | |
| NM_003754 | EIF3S5 | Homo sapiens eukaryotic translation initiation factor 3, subunit 5 epsilon, 47kDa (EIF3S5), mRNA. | |

Figure 22 (2)

| Gene Symbol | | Nucleotide Sequence Description | |
|----------------------------|-------------------------------|--|--|
| GenBank Accession for mRNA | GenBank Accession for Protein | | |
| XM_012968 | XP_012968 | Homo sapiens similar to chromosome 20 open reading frame 14; putative mitochondrial outer membrane protein import receptor, similar to yeast pre-mRNA splicing factors, Prp1/Zer and Prp6 (LOC151921), mRNA. | |
| NM_004593 | NP_004584 | Homo sapiens splicing factor, arginine/serine-rich 10 (transformer 2 homolog, Drosophila) (SFRS10), mRNA. | |
| NM_017489 | NP_059523 | Homo sapiens telomeric repeat binding factor (NIMA-interacting) 1 (TERF1), transcript variant 1, mRNA. | |
| NM_020143 | NP_064528 | Homo sapiens putative 28 kDa protein (LOC56902), mRNA. | |
| XM_067072 | XP_067072 | Homo sapiens similar to RBM1 (LOC140098), mRNA. | |
| XM_059656 | XP_059656 | Homo sapiens similar to PGC-1 related co-activator (LOC133522), mRNA. | |
| X99302 | CAA67684 | H. sapiens mRNA for Pop1 protein. | |
| AL080063 | CAB45694 | Homo sapiens mRNA; cDNA DKFZp564I052 (from clone DKFZp564I052). | |
| NM_006112 | NP_006103 | Homo sapiens peptidylprolyl isomerase E (cyclophilin E) (PPIE), transcript variant 1, mRNA. | |
| _005826 | NP_005817 | Homo sapiens heterogeneous nuclear ribonucleoprotein R (HNRPR), mRNA. | |
| _003819 | NP_003810 | Homo sapiens poly(A) binding protein, cytoplasmic 4 (inducible form) (PABPC4), mRNA. | |
| _003690 | NP_003681 | Homo sapiens protein kinase, interferon-inducible double stranded RNA dependent activator (PRKRA), mRNA. | |
| _001488 | NP_001479 | Homo sapiens transcriptional adaptor 2 (ADA2 homolog, yeast)-like (TADA2L), transcript variant 1, mRNA. | |
| 058653 | XP_058653 | Homo sapiens LOC122651 (LOC122651), mRNA. | |
| _004953 | NP_004944 | Homo sapiens eukaryotic translation initiation factor 4 gamma, 1 (EIF4G1), transcript variant 5, mRNA. | |
| _088868 | XP_088868 | Homo sapiens LOC163412 (LOC163412), mRNA. | |
| _021038 | NP_066368 | Homo sapiens muscleblind-like (Drosophila) (MBNL1), mRNA. | |
| _017736 | NP_060206 | Homo sapiens hypothetical protein FLJ20274 (FLJ20274), mRNA. | |
| NM_006451 | NP_006442 | Homo sapiens poly(A) binding protein interacting protein 1 (PAIP1), transcript variant 1, mRNA. | |
| NM_004501 | NP_004492 | Homo sapiens heterogeneous nuclear ribonucleoprotein U (scaffold attachment factor A) (HNRPU), transcript variant 2, mRNA. | |
| NM_001412 | NP_001403 | Homo sapiens eukaryotic translation initiation factor 1A (EIF1A), mRNA. | |
| AB014564 | BAA31639 | Homo sapiens mRNA for KIAA0664 protein, partial cds. | |
| D80007 | BAA11502 | Homo sapiens KIAA0185 mRNA, complete cds. | |
| NM_004184 | NP_004175 | Homo sapiens tryptophanyl-tRNA synthetase (WARS), mRNA. | |
| NM_019038 | NP_061911 | Homo sapiens tudor domain containing 4 (TDRD4), mRNA. | |
| NM_030621 | NP_085124 | Homo sapiens Dicer1, Dcr-1 homolog (Drosophila) (DICER1), transcript variant 2, mRNA. | |
| AF167570 | AAD51099 | Homo sapiens nuclear factor associated with dsRNA NFAR-2 mRNA, complete cds. | |
| NM_005872 | NP_005863 | Homo sapiens breast carcinoma amplified sequence 2 (BCAS2), mRNA. | |

Figure 22 (3)

| Gene Symbol | | Nucleotide Sequence Description | |
|----------------------------------|-------------------------------------|--|--|
| GenBank Accession for mRNA | GenBank Accession for Protein | | |
| D82351 | BAA11561 | Human retropseudogene MSSP-1 DNA, complete cds. | |
| NM_004990 | NP_004981 | Homo sapiens methionine-tRNA synthetase (MARS), mRNA. | |
| NM_006842 | NP_006833 | Homo sapiens splicing factor 3b, subunit 2, 145kD (SF3B2), mRNA | |
| NM_017840 | NP_060310 | Homo sapiens mitochondrial ribosomal protein L16 (MRPL16), nuclear gene encoding mitochondrial protein, mRNA | |

Figure 22(4)

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | Description |
|--|--|---|---|
| AB000280 | PHT1 | BAA20489 | Rattus norvegicus mRNA for peptide/histidine transporter, complete cds. |
| AB011679 | | BAA32736 | Rattus norvegicus mRNA for class I beta-tubulin, complete cds. |
| AB017265 | | BAA82585 | Rattus norvegicus gene for glycosylphosphatidylinositol anchor attachment 1 (GPAA1), partial cds. |
| AB018253 | | BAA76556 | Rattus norvegicus mRNA for voltage-gated ca channel, complete cds. |
| AB045586 | cmr5 | BAB61764 | Rattus norvegicus cmr5 mRNA for cadherin-related neuronal receptor 5, partial cds. |
| AB047324 | TAT1 | BAB55595 | Rattus norvegicus TAT1 mRNA, complete cds. |
| AB054997 | | BAB2175 | Rattus norvegicus mRNA for QKI, partial cds. |
| AF003187 | | AAB60895 | Rattus norvegicus cocaine attenuated zinc-finger protein mRNA, partial cds. |
| AF022089 | | AAB82556 | Rattus norvegicus guanine nucleotide binding protein gamma 4 subunit mRNA, partial cds. |
| AF022091 | | AAB82558 | Rattus norvegicus guanine nucleotide binding protein gamma 12 subunit mRNA, partial cds. |
| AF028604 | P2X2 | AAC72286 | Rattus norvegicus P2X2 purinoceptor isoform f (P2X2) mRNA, partial cds. |
| AF035952 | Krp3a | AAB88700 | Rattus norvegicus khesin-related protein 3A (Krp3a) mRNA, partial cds. |
| AF050159 | IRS-2 | AAC05512 | Rattus norvegicus insulin receptor substrate 2 (IRS-2) mRNA, partial cds. |
| AF061443 | LGR4 | AAC77910 | Rattus norvegicus G protein-coupled receptor LGR4 (LGR4) mRNA, complete cds. |
| AF079162 | plc | AAC99398 | Rattus norvegicus patched (plc) mRNA, partial cds. |
| AF083418 | IRS-2 | AAC33346 | Rattus norvegicus insulin receptor substrate-2 (IRS-2) mRNA, partial cds. |
| AF087674 | IRS-2 | AAC36726 | Rattus norvegicus insulin receptor substrate 2 (IRS-2) mRNA, partial cds. |
| AF102262 | beta1-4GT | AAD41721 | Rattus norvegicus N-acetylglucosamine galactosyltransferase (beta1-4GT) mRNA, partial cds. |
| AF109644 | CAR1 | AAF01255 | Rattus norvegicus coxsackie-adenovirus-receptor homolog (CAR1) mRNA, partial cds. |
| AF130341 | MT1 | AAG18471 | Rattus norvegicus melatonin receptor (MT1) mRNA, partial cds. |
| AF136231 | | AAD33684 | Rattus norvegicus caspase-2 mRNA, complete cds. |
| AF148323 | APPLS | AAF73106 | Rattus norvegicus aminopeptidase PLS (APPLS) mRNA, complete cds. |
| AF159049 | | AAF80364 | Rattus norvegicus angiotensin II type 1A receptor associated protein mRNA, complete cds. |
| AF186469 | TM6P1 | AAF01324 | Rattus norvegicus TM6P1 (TM6P1) mRNA, complete cds. |
| AF189261 | Theta | AAF70382 | Rattus norvegicus GABA-A receptor theta subunit (Theta) mRNA, partial cds. |

Figure 23

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | Description |
|--|--|---|--|
| AF195045 | | AAF28720 | Rattus norvegicus TRC8 gene, partial cds. |
| AF200359 | Ugt1 | AAF67072 | Rattus norvegicus UDP-glucose glycoprotein:glucosyltransferase precursor (Ugt1) mRNA, complete cds. |
| AF228043 | | AAF76422 | Rattus norvegicus nuclear hormone receptor co-regulator/co-activator mRNA, partial cds. |
| AF239219 | Pgt2 | AAK15063 | Rattus norvegicus prostaglandin transporter subtype 2 (Pgt2) mRNA, complete cds. |
| AF244920 | | AAF44715 | Rattus norvegicus potassium channel regulatory factor mRNA, complete cds. |
| AF260582 | | AAK49395 | Rattus norvegicus hippygranin mRNA, complete cds. |
| AF268030 | | AAF72546 | Rattus norvegicus copper transporter 1 mRNA, complete cds. |
| AF273024 | | AAF81786 | Rattus norvegicus amino acid system A transporter mRNA, complete cds. |
| AF352172 | | AAK32708 | Rattus norvegicus v-rat murine sarcoma viral oncogene B1-like protein mRNA, partial cds. |
| AF361239 | | AAK67316 | Rattus norvegicus lysosomal amino acid transporter 1 mRNA, complete cds. |
| AF385409 | Elf5a2 | AAL40650 | Rattus norvegicus eukaryotic translation initiation factor 5A isoform II (Elf5a2) gene, exons 2 and 3 and partial cds. |
| AF385833 | | AAK66567 | Rattus norvegicus RAC1 mRNA, partial cds. |
| AF406814 | | AAK96221 | Rattus norvegicus clone PLRR-4 polymorphic leucine-rich repeat protein mRNA, complete cds. |
| AF439397 | Sip30 | AAL35221 | Rattus norvegicus SNAP25 interacting protein 30 (Sip30) mRNA, complete cds. |
| AF441118 | Bnip3l | AAL32462 | Rattus norvegicus BNIP3L protein (Bnip3l) mRNA, complete cds. |
| AF442357 | | AAL35353 | Rattus norvegicus reticulon 3 protein isoform a mRNA, complete cds; alternatively spliced. |
| AJ131111 | LANCL1 | CAB63943 | Rattus sp. mRNA lanthionine synthetase C-like protein 1 (LANCL1 gene). |
| AJ224156 | | CAA11853 | Rattus norvegicus mRNA for ceramide glucosyltransferase. |
| AJ243395 | scn3b | CAB76838 | Rattus norvegicus mRNA for voltage-gated sodium channel beta-3 subunit. |
| AY012054 | Zfx | AAG38797 | Rattus norvegicus zinc finger protein ZFX (Zfx) gene, partial cds. |
| D14418 | PP2A ARa | BAA21903 | Rattus norvegicus PP2A ARa mRNA for A regulatory subunit of protein phosphatase 2A, partial cds. |
| D16479 | RTP-beta | BAA03940 | Rat mRNA for mitochondrial long-chain 3-ketacyl-CoA thioase beta-subunit of mitochondrial trifunctional protein, complete cds. |
| D17521 | CIC-3 | BAA04471 | Rattus rattus CIC-3 mRNA for protein kinase C-regulated chloride channel, complete cds. |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | Description |
|--|--|---|---|
| D25233 | | BAA04958 | Rattus norvegicus mRNA for retinoblastoma protein, partial sequence. |
| J02934 | | AAA41856 | Rat cAMP-dependent protein kinase type II regulatory subunit mRNA, 3' end. |
| J04963 | | AAA41104 | Rat ecto-ATPase mRNA, complete cds. |
| L09752 | VIN1 | AAA41010 | Rat cyclin D2 (VIN1) mRNA, complete cds. |
| L10639 | ActRII | AAA40674 | Rat activin type II receptor (ActRII) mRNA, 5' end of cds. |
| L12382 | | AAA40687 | Rattus norvegicus ADP-ribosylation factor 3 mRNA, complete cds. |
| L22761 | GATA-GT2 | AAA416159 | Rat DNA binding protein (GATA-GT2) mRNA, complete cds. |
| M18331 | | AAA41872 | Rat protein kinase C epsilon subspecies. |
| M18769 | | AAA41196 | Rat liver beta-galactoside alpha 2,6-sialyltransferase mRNA, complete cds. |
| M19042 | | AAA41626 | Rat proviral Moloney murine leukemia mutant in 594-2 DNA, partial cds. |
| M24353 | | AAA66457 | Rat proviral Moloney murine leukemia mutant in 594-2 DNA, partial cds. |
| M32973 | | AAA41639 | Rattus norvegicus alpha-mannosidase II mRNA, partial cds. |
| M34083 | | AAA79273 | Rat mitochondrial solute carrier protein mRNA, 5' end. |
| M35965 | | AAA42089 | Rat lactogen receptor mRNA, complete cds. |
| M55292 | tkB | AAA42280 | Rat thyroglobulin (rTg-2) mRNA, complete cds. |
| NM_012506 | Alp1a3 | NP_036638 | Rattus norvegicus protein-tyrosine kinase (trkB) mRNA, complete cds. |
| NM_012551 | Egr1 | NP_036683 | Rattus norvegicus ATPase, Na ⁺ /K ⁺ transporting, alpha 3 polypeptide (Alp1a3), mRNA. |
| NM_012563 | Gad2 | NP_036695 | Rattus norvegicus early growth response 1 (Egr1), mRNA. |
| NM_012569 | Gls | NP_036701 | Rattus norvegicus glutamate decarboxylase 2 (Gad2), mRNA. |
| NM_012609 | Nf1 | NP_036741 | Rattus norvegicus glutaminase (Gls), mRNA. |
| NM_012637 | Ptgn1 | NP_036769 | Rattus norvegicus neurofibromatosis 1 (Nf1), mRNA. |
| NM_012649 | Sdc4 | NP_036781 | Rattus norvegicus protein tyrosine phosphatase, non-receptor type 1 (Ptgn1), mRNA. |
| NM_012655 | Sp1 | NP_036787 | Rattus norvegicus syndecan 4 (Sdc4), mRNA. |
| NM_012663 | Vamp2 | NP_036795 | Rattus norvegicus Sp1 transcription factor (Sp1), mRNA. |
| NM_012713 | Pkcb1 | NP_036845 | Rattus norvegicus vesicle-associated membrane protein 2 (Vamp2), mRNA. Rattus norvegicus protein kinase C, beta 1 (Pkcb1), mRNA. |

| Nucleotide GenBank Accession Number or Manufacturer | Gene Name or Manufacturer | Probe Name | Protein Product | |
|---|------------------------------|------------|---|--|
| | | | GeneBank Accession Number or Manufacturer | Description |
| NM_012794 | Glycam1 | | NP_036926 | Rattus norvegicus glycosylation dependent cell adhesion molecule 1 (Glycam1), mRNA. |
| NM_012799 | Nmbr | | NP_036931 | Rattus norvegicus neuromedin B receptor (Nmbr), mRNA. |
| NM_012806 | Mapk10 | | NP_036938 | Rattus norvegicus mitogen activated protein kinase 10 (Mapk10), mRNA. |
| NM_012836 | Cpd | | NP_036968 | Rattus norvegicus carboxypeptidase D (Cpd), mRNA. |
| NM_012863 | Mist1 | | NP_036995 | Rattus norvegicus muscle, intestine and stomach expression 1 (Mist1), mRNA. |
| NM_012879 | Sic2a2 | | NP_037011 | Rattus norvegicus solute carrier family 2, member 2 (Sic2a2), mRNA. |
| NM_012919 | Cacna2d1 | | NP_037051 | Rattus norvegicus calcium channel, voltage-dependent, alpha2/delta subunit 1 (Cacna2d1), mRNA. |
| NM_012948 | Emd | | NP_037080 | Rattus norvegicus emerin (Emd), mRNA. |
| NM_012998 | P4hb | | NP_037130 | Rattus norvegicus prolyl 4-hydroxylase, beta polypeptide (P4hb), mRNA. |
| NM_013029 | Sial8c | | NP_037161 | Rattus norvegicus sialyltransferase 8 C (Sial8c), mRNA. |
| NM_013038 | Sxbp1 | | NP_037170 | Rattus norvegicus syntaxin binding protein 1 (Sxbp1), mRNA. |
| NM_013080 | Piprz1 | | NP_037212 | Rattus norvegicus protein tyrosine phosphatase, receptor-type, Z polypeptide 1 (Piprz1), mRNA. |
| NM_013087 | Cd81 | | NP_037219 | Rattus norvegicus CD 81 antigen (Cd81), mRNA. |
| NM_013123 | Il1r1 | | NP_037255 | Rattus norvegicus interleukin 1 receptor, type I (Il1r1), mRNA. |
| NM_013159 | Ide | | NP_037291 | Rattus norvegicus insulin degrading enzyme (Ide), mRNA. |
| NM_013181 | Prkar1a | | NP_037313 | Rattus norvegicus protein kinase, cAMP dependent regulatory, type I, alpha (Prkar1a), mRNA. |
| NM_016999 | Cyp4b1 | | NP_058695 | Rattus norvegicus cytochrome P450, subfamily 4B, polypeptide 1 (Cyp4b1), mRNA. |
| NM_017065 | Gabrb3 | | NP_058761 | Rattus norvegicus gamma-aminobutyric acid receptor, subunit beta 3 (Gabrb3), mRNA. |
| NM_017091 | Pcsk1 | | NP_058787 | Rattus norvegicus proprotein convertase subtilisin/kexin type 1 (Pcsk1), mRNA. |
| NM_017135 | Ak4 | | NP_058831 | Rattus norvegicus adenylate kinase 4 (Ak4), mRNA. |
| NM_017197 | Cugbp2 | | NP_058893 | Rattus norvegicus CUG triplet repeat RNA-binding protein 2 (Cugbp2), mRNA. |
| NM_017206 | Sic6a6 | | NP_058902 | Rattus norvegicus solute carrier family 6, member 6 (Sic6a6), mRNA. |
| NM_017231 | Pitpn | | NP_058927 | Rattus norvegicus phosphatidylinositol transfer protein (Pitpn), mRNA. |
| NM_017269 | Ptpj | | NP_058965 | Rattus norvegicus protein tyrosine phosphatase, receptor type, J (Ptpj), mRNA. |
| NM_017322 | Mapk9 | | NP_059018 | Rattus norvegicus stress activated protein kinase alpha II (Mapk9), mRNA. |

Figure 23

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | | Description |
|--|--|---|---|-------------|
| | | | | |
| NM_017323 | Tr4 | NP_059019 | Rattus norvegicus TR4 orphan receptor (Tr4), mRNA. | |
| NM_017348 | CHOT1 | NP_059044 | Rattus norvegicus choline transporter (CHOT1), mRNA. | |
| NM_019142 | Prkaa1 | NP_062015 | Rattus norvegicus protein kinase, AMP-activated, alpha 1 catalytic subunit (Prkaa1), mRNA. | |
| NM_019166 | Syng1 | NP_062039 | Rattus norvegicus synaptophysin 1 (Syng1), mRNA. | |
| NM_019182 | Rnf4 | NP_062055 | Rattus norvegicus ring finger protein 4 (Rnf4), mRNA. | |
| NM_019192 | Sepp1 | NP_062065 | Rattus norvegicus selenoprotein P, plasma, 1 (Sepp1), mRNA. | |
| NM_019195 | Cd47 | NP_062068 | Rattus norvegicus integrin-associated protein (Cd47), mRNA. | |
| NM_019248 | Nlrk3 | NP_062121 | Rattus norvegicus neural receptor protein-tyrosine kinase (Nlrk3), mRNA. | |
| NM_019275 | Madh4 | NP_062148 | Rattus norvegicus MAD homolog 4 (Drosophila) (Madh4), mRNA. | |
| NM_019354 | Ucp2 | NP_062227 | Rattus norvegicus uncoupling protein 2 (Ucp2), mRNA. | |
| NM_019367 | Ppt2 | NP_062240 | Rattus norvegicus palmitoyl-protein thioesterase 2 (Ppt2), mRNA. | |
| NM_019377 | Ywhab | NP_062250 | Rattus norvegicus tyrosine 3-monooxygenase/tryptophan 5 monooxygenase activation protein, beta polypeptide (Ywhab), mRNA. | |
| NM_021594 | LOC59114 | NP_067605 | Rattus norvegicus ERM-binding phosphoprotein (LOC59114), mRNA. | |
| NM_021597 | Gerp95 | NP_067608 | Rattus norvegicus GERP95 (Gerp95), mRNA. | |
| NM_021671 | LOC59303 | NP_067703 | Rattus norvegicus db83 (LOC59303), mRNA. | |
| NM_021680 | Nxph4 | NP_067712 | Rattus norvegicus neurexophilin 4 (Nxph4), mRNA. | |
| NM_021682 | LOC59318 | NP_067714 | Rattus norvegicus kilon (LOC59318), mRNA. | |
| NM_021851 | Ltn7c | NP_068623 | Rattus norvegicus lin-7-C (Ltn7c), mRNA. | |
| NM_022005 | Fxyd6 | NP_071288 | Rattus norvegicus FXD domain-containing ion transport regulator 6 (Fxyd6), mRNA. | |
| NM_022208 | Gtf2a1 | NP_071544 | Rattus norvegicus general transcription factor 2a, 1 (Gtf2a1), mRNA. | |
| NM_022223 | Fgf14 | NP_071559 | Rattus norvegicus fibroblast growth factor 14 (Fgf14), mRNA. | |
| NM_022231 | Birc4 | NP_071567 | Rattus norvegicus baculoviral IAP repeat-containing 4 (Birc4), mRNA. | |
| NM_022386 | Matg | NP_071781 | Rattus norvegicus v-maf musculoaponeurotic fibrosarcoma (avian) oncogene family, protein G (Matg), mRNA. | |

Figure 23

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | | Description |
|--|--|---|-----------|--|
| | | Pafah1b2 | NP_071782 | |
| NM_022387 | | | | Rattus norvegicus platelet-activating factor acetylhydrolase alpha 2 subunit (PAF-AH alpha 2) (Pafah1b2), mRNA. |
| NM_022396 | Gng11 | | NP_071791 | Rattus norvegicus guanine nucleotide binding protein gamma subunit 11 (Gng11), mRNA. |
| NM_022502 | Ppt | | NP_071947 | Rattus norvegicus palmitoyl-protein thioesterase (Ppt), mRNA. |
| NM_022516 | Ptb | | NP_071961 | Rattus norvegicus polypyrimidine tract binding protein (Ptb), mRNA. |
| NM_022522 | Casp2 | | NP_071967 | Rattus norvegicus caspase 2 (Casp2), mRNA. |
| NM_022548 | PAG608 | | NP_071993 | Rattus norvegicus p53-activated gene 608 (PAG608), mRNA. |
| U_022612 | Bcl2l1 | | NP_072134 | Rattus norvegicus BCL2-like 11 (apoptosis facilitator) (Bcl2l1), transcript variant 1, mRNA. |
| U_022619 | Slc7a2 | | NP_072141 | Rattus norvegicus solute carrier family 7, member 3 (Slc7a2), mRNA. |
| U_022673 | Mecp2 | | NP_073164 | Rattus norvegicus methyl CpG binding protein 2 (Mecp2), mRNA. |
| U_022799 | Nucks | | NP_073636 | Rattus norvegicus nuclear ubiquitous casein kinase 2 (Nucks), mRNA. |
| U_022931 | Nim3 | | NP_075220 | Rattus norvegicus nim3 protein (Nim3), mRNA. |
| U_022950 | C1gal1 | | NP_075239 | Rattus norvegicus core 1 UDP-galactose:N-acetylgalactosamine-alpha-R beta 1,3-galactosyltransferase (C1gal1) (C1gal1), mRNA. |
| M_023095 | Mgal5 | | NP_075583 | Rattus norvegicus N-acetylglucosaminyltransferase V (Mgal5), mRNA. |
| M_023956 | Gucy1a2 | | NP_076446 | Rattus norvegicus soluble guanylyl cyclase alpha2 subunit (Gucy1a2), mRNA. |
| M_023977 | Gmx33 | | NP_076467 | Rattus norvegicus trans-Golgi protein Gmx33 (Gmx33), mRNA. |
| NM_023991 | Pkaa2 | | NP_076481 | Rattus norvegicus protein kinase, AMP-activated, alpha 2 catalytic subunit (Pkaa2), mRNA. |
| NM_024132 | Faah | | NP_077046 | Rattus norvegicus fatty acid amide hydrolase (Faah), mRNA. |
| NM_024139 | Chp | | NP_077053 | Rattus norvegicus calcium binding protein p22 (Chp), mRNA. |
| NM_024158 | Dck | | NP_077072 | Rattus norvegicus deoxycytidine kinase (Dck), mRNA. |
| NM_024368 | Frk | | NP_077344 | Rattus norvegicus src related tyrosine kinase (Frk), mRNA. |
| NM_024370 | Gabrg3 | | NP_077346 | Rattus norvegicus GABA-alpha receptor gamma-3 subunit (Gabrg3), mRNA. |
| NM_024374 | Mipn | | NP_077350 | Rattus norvegicus myotrophin (Mipn), mRNA. |
| NM_030586 | omb5 | | NP_085075 | Rattus norvegicus cytochrome b5, outer mitochondrial membrane isoform (omb5), mRNA. |

Figure 23

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank | | Description |
|--|--|---|-----------|--|
| | | Accession Number or Manufacturer Sequence | Reference | |
| NM_030829 | Gpr5 | NP_110456 | | Rattus norvegicus G protein-coupled receptor kinase 5 (Gpr5), mRNA. |
| NM_030835 | RAMP4 | NP_110462 | | Rattus norvegicus ribosome associated membrane protein 4 (RAMP4), mRNA. |
| NM_030849 | Bmpr1a | NP_110476 | | Rattus norvegicus bone morphogenetic protein receptor, type 1A (Bmpr1a), mRNA. |
| NM_030873 | Pln2 | NP_110500 | | Rattus norvegicus profilin II (Pln2), mRNA. |
| NM_030991 | Snap25 | NP_112253 | | Rattus norvegicus synaptosomal-associated protein (Snap25), mRNA. |
| NM_031011 | Amd1 | NP_112273 | | Rattus norvegicus S-adenosylmethionine decarboxylase 1 (Amd1), mRNA. |
| NM_031031 | Gatm | NP_112293 | | Rattus norvegicus glycine amidinotransferase (L-arginine:glycine amidinotransferase) (Gatm), mRNA. |
| NM_031034 | Gna12 | NP_112296 | | Rattus norvegicus guanine nucleotide binding protein, alpha 12 (Gna12), mRNA. |
| NM_031036 | Gnaq | NP_112298 | | Rattus norvegicus heterotrimeric guanine nucleotide-binding protein alpha q subunit (Gnaq), mRNA. |
| NM_031049 | Lss | NP_112311 | | Rattus norvegicus 2,3-oxidosqualene: lanosterol cyclase (Lss), mRNA. |
| NM_031057 | Mmsdh | NP_112319 | | Rattus norvegicus methylmalonate semialdehyde dehydrogenase gene (Mmsdh), mRNA. |
| NM_031061 | Musk | NP_112323 | | Rattus norvegicus muscle, skeletal, receptor tyrosine kinase (Musk), mRNA. |
| NM_031079 | Pde2a | NP_112341 | | Rattus norvegicus phosphodiesterase 2A, cGMP-stimulated (Pde2a), mRNA. |
| NM_031081 | Pdpk1 | NP_112343 | | Rattus norvegicus 3-phosphoinositide dependent protein kinase-1 (Pdpk1), mRNA. |
| NM_031120 | Ssr3 | NP_112382 | | Rattus norvegicus TRAP-complex gamma subunit (Ssr3), mRNA. |
| NM_031123 | Sic1 | NP_112385 | | Rattus norvegicus stanniocalcin 1 (Sic1), mRNA. |
| NM_031143 | Dgkz | NP_112405 | | Rattus norvegicus diacylglycerol kinase zeta (Dgkz), mRNA. |
| NM_031152 | Rab11a | NP_112414 | | Rattus norvegicus RAB11a, member RAS oncogene family (Rab11a), mRNA. |
| NM_031344 | Fads2 | NP_112634 | | Rattus norvegicus fatty acid desaturase 2 (Fads2), mRNA. |
| NM_031346 | Rod1 | NP_112636 | | Rattus norvegicus regulator of differentiation (in S. pombe) 1 (Rod1), mRNA. |
| NM_031515 | Kras2 | NP_113703 | | Rattus norvegicus Kirsten rat sarcoma viral oncogene homolog 2 (active) (Kras2), mRNA. |
| NM_031521 | Ncam1 | NP_113709 | | Rattus norvegicus neural cell adhesion molecule 1 (Ncam1), mRNA. |
| NM_031528 | Rara | NP_113716 | | Rattus norvegicus retinoic acid receptor, alpha (Rara), mRNA. |
| NM_031575 | Akt3 | NP_113763 | | Rattus norvegicus thymoma viral proto-oncogene 3 (Akt3), mRNA. |
| NM_031593 | Sv2c | NP_113781 | | Rattus norvegicus synaptic vesicle protein 2C (Sv2c), mRNA. |

Figure 23

| Nucleotide GenBank Accession Number or Manufacturer | Gene Name or Manufacturer | Protein Product GeneBank | | Description |
|---|------------------------------|-------------------------------------|-----------------------|--|
| | | Accession Number or Manufacturer | Sequence Reference | |
| NM_031604 | Alp6n1a | NP_113792 | | Rattus norvegicus ATPase, H+ transporting, lysosomal noncatalytic accessory protein 1a (Alp6n1a), mRNA. |
| NM_031605 | Cyp4a12 | NP_113793 | | Rattus norvegicus cytochrome P450, 4a12 (Cyp4a12), mRNA. |
| NM_031615 | Znf148 | NP_113803 | | Rattus norvegicus zinc finger protein 148 (Znf148), mRNA. |
| NM_031726 | Scamp5 | NP_113914 | | Rattus norvegicus secretory carrier membrane protein 5 (Scamp5), mRNA. |
| NM_031751 | Shank1 | NP_113939 | | Rattus norvegicus Shank1 (Shank1), mRNA. |
| NM_031755 | Ceacam1 | NP_113943 | | Rattus norvegicus carcinoembryonic antigen-related cell adhesion molecule 1 (Ceacam1), mRNA. |
| NM_031757 | Mmp24 | NP_113945 | | Rattus norvegicus matrix metalloproteinase 24 (membrane-inserted) (Mmp24), mRNA. |
| NM_031785 | Alp6s1 | NP_113973 | | Rattus norvegicus ATPase, H+ transporting, lysosomal (vacuolar proton pump), subunit 1 (Alp6s1), mRNA. |
| NM_031787 | Hipk3 | NP_113975 | | Rattus norvegicus homeodomain-interacting protein kinase 3 (Hipk3), mRNA. |
| NM_031812 | Cd164 | NP_114000 | | Rattus norvegicus CD164 antigen (Cd164), mRNA. |
| NM_031818 | Clic4 | NP_114006 | | Rattus norvegicus chloride intracellular channel 4 (Clic4), mRNA. |
| NM_031828 | Kcnma1 | NP_114016 | | Rattus norvegicus potassium large conductance calcium-activated channel, subfamily M, alpha member 1 (Kcnma1), mRNA. |
| NM_031841 | Scd2 | NP_114029 | | Rattus norvegicus stearoyl-Coenzyme A desaturase 2 (Scd2), mRNA. |
| NM_031986 | Sdcbp | NP_114192 | | Rattus norvegicus syntrophin (Sdcbp), mRNA. |
| NM_032080 | Gsk3b | NP_114469 | | Rattus norvegicus glycogen synthase kinase 3 beta (Gsk3b), mRNA. |
| NM_032084 | Chn2 | NP_114473 | | Rattus norvegicus chimerin (chimaerin) 2 (Chn2), mRNA. |
| NM_033376 | Kcnk3 | NP_203694 | | Rattus norvegicus potassium channel, subfamily K, member 3 (Kcnk3), mRNA. |
| NM_052801 | Vhl | NP_434688 | | Rattus norvegicus von Hippel-Lindau syndrome homolog (Vhl), mRNA. |
| NM_053308 | Fkbp2 | NP_445760 | | Rattus norvegicus FK506 binding protein 2 (Fkbp2), mRNA. |
| NM_053342 | Idax | NP_445794 | | Rattus norvegicus inhibitor of the Dvl and Axin complex (Idax), mRNA. |
| NM_053352 | Rdc1 | NP_445804 | | Rattus norvegicus chemokine orphan receptor 1 (Rdc1), mRNA. |
| NM_053379 | Dcx | NP_445831 | | Rattus norvegicus doublecortin (Dcx), mRNA. |
| NM_053407 | Asah | NP_445859 | | Rattus norvegicus N-acylsphingosine amidohydrolase (acid ceramidase) (Asah), mRNA. |
| NM_053424 | Sic4a4 | NP_445876 | | Rattus norvegicus solute carrier family 4, member 4 (Sic4a4), mRNA. |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | | Description |
|--|--|--|--------|--|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | Slc7a8 | |
| NM_053442 | | NP_445894 | | Rattus norvegicus solute carrier family 7 (cationic amino acid transporter, y ⁺ system), member 8 (Slc7a8), mRNA. |
| NM_053445 | Fads1 | NP_445897 | | Rattus norvegicus fatty acid desaturase 1 (Fads1), mRNA. |
| NM_053465 | Fut9 | NP_445917 | | Rattus norvegicus fucosyltransferase 9 (alpha (1,3) fucosyltransferase) (Fut9), mRNA. |
| NM_053467 | Tmp21 | NP_445919 | | Rattus norvegicus integral membrane protein Tmp21-1 (p23) (Tmp21), mRNA. |
| NM_053472 | Cox4b | NP_445924 | | Rattus norvegicus cytochrome c oxidase, subunit 4b (Cox4b), mRNA. |
| NM_053486 | Kif3c | NP_445938 | | Rattus norvegicus kinesin family member 3C (Kif3c), mRNA. |
| NM_053494 | Slc2a8 | NP_445946 | | Rattus norvegicus solute carrier family 2, (facilitated glucose transporter) member 8 (Slc2a8), mRNA. |
| NM_053502 | Abcg1 | NP_445954 | | Rattus norvegicus ATP-binding cassette, sub-family G (WHITE), member 1 (Abcg1), mRNA. |
| NM_053565 | Cish3 | NP_446017 | | Rattus norvegicus cytokine inducible SH2-containing protein 3 (Cish3), mRNA. |
| NM_053578 | Alp6k | NP_446030 | | Rattus norvegicus vacuolar proton-ATPase subunit M9.2 (Alp6k), mRNA. |
| NM_053589 | Rab14 | NP_446041 | | Rattus norvegicus GTPase Rab14 (Rab14), mRNA. |
| NM_053646 | Asah2 | NP_446098 | | Rattus norvegicus N-acylsphingosine amidohydrolase 2 (Asah2), mRNA. |
| NM_053714 | Ank | NP_446166 | | Rattus norvegicus progressive ankylosis (Ank), mRNA. |
| NM_053722 | Clasp2 | NP_446174 | | Rattus norvegicus CLIP-associated protein 2 (Clasp2), mRNA. |
| NM_053770 | Argbp2 | NP_446222 | | Rattus norvegicus Arg/Abi-interacting protein ArgBP2 (Argbp2), mRNA. |
| NM_053794 | Prkwnk1 | NP_446246 | | Rattus norvegicus protein kinase, lysine deficient 1 (Prkwnk1), mRNA. |
| NM_053798 | Sacm1l | NP_446250 | | Rattus norvegicus SAC1 (suppressor of actin mutations 1, homolog)-like (S. cerevisiae) (Sacm1l), mRNA. |
| NM_053863 | Slc28a1 | NP_446315 | | Rattus norvegicus solute carrier family 28 (sodium-coupled nucleoside transporter), member 1 (Slc28a1), mRNA. |
| NM_053886 | Lman1 | NP_446338 | | Rattus norvegicus lectin, mannose-binding, 1 (Lman1), mRNA. |
| NM_053891 | Cdk5r | NP_446343 | | Rattus norvegicus cyclin-dependent kinase 5, regulatory subunit 1 (p35) (Cdk5r), mRNA. |
| NM_053952 | Nup155 | NP_446404 | | Rattus norvegicus nucleoporin 155kD (Nup155), mRNA. |
| NM_054000 | Kcnb2 | NP_446452 | | Rattus norvegicus potassium voltage gated channel, Shab-related subfamily, member 2 (Kcnb2), mRNA. |
| NM_057098 | Tcea2 | NP_476439 | | Rattus norvegicus transcription elongation factor A2 (Tcea2), mRNA. |

Figure 23

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | | Description |
|--|--|--|--|--|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | GeneBank Accession Number or Manufacturer Sequence Reference | |
| NM_057132 | Aha2 | NP_476473 | | Rattus norvegicus p13ras-related homolog A2 (Aha2), mRNA. |
| NM_057148 | 2-Sep | NP_476489 | | Rattus norvegicus septin 2 (Sep2), mRNA. |
| NM_057186 | Hadhsc | NP_476534 | | Rattus norvegicus L-3-hydroxyacyl-Coenzyme A dehydrogenase, short chain (Hadhsc), mRNA. |
| NM_057210 | Sv2a | NP_476558 | | Rattus norvegicus synaptic vesicle glycoprotein 2 a (Sv2a), mRNA. |
| NM_080577 | Npl4 | NP_542144 | | Rattus norvegicus homolog of yeast nuclear protein localization 4 (Npl4), mRNA. |
| S61973 | | AAB20211 | | Rattus sp. NMDA receptor glutamate-binding subunit mRNA, complete cds. |
| S73608 | AGR9 | AAB31153 | | AGR9=G protein-coupled receptor [rats, aortic vascular smooth muscle cells, mRNA, 1601 nt]. |
| U07795 | rap1B | AAA92787 | | Rattus norvegicus Rap1B mRNA, complete cds. |
| U15408 | | AAA81005 | | Rattus norvegicus plasma membrane Ca2+-ATPase isoform 4 mRNA, complete cds and alternatively spliced variations. |
| U21116 | | AAA96350 | | Rattus norvegicus rSec1B mRNA, complete cds. |
| U31815 | ROB2 | AAA89157 | | Rattus norvegicus calcium channel alpha-1C subunit (ROB2) mRNA, partial cds. |
| U39572 | | AAD10400 | | Rattus norvegicus phosphatidylinositol 4-kinase mRNA, complete cds. |
| U40188 | DN-7 | AAC53201 | | Rattus norvegicus neuronal cell death related gene in neuron-7 (DN-7) mRNA, complete cds. |
| U41183 | GHRH | AAC53041 | | Rattus norvegicus placental pre-progrowth hormone-releasing hormone (GHRH) mRNA, complete cds. |
| U41853 | ORP150 | AAB05672 | | Rattus norvegicus 150 kDa oxygen regulated protein (ORP150) mRNA, complete cds. |
| U53927 | | AAC52813 | | Rattus norvegicus brain astroglial high-affinity cationic amino acid transporter RCAT2 mRNA, partial cds. |
| U56261 | | AAA99825 | | Rattus norvegicus SNAP-25a mRNA, partial cds. |
| U61772 | NF2 | AAC13318 | | Rattus norvegicus merlin (NF2) mRNA, partial cds. |
| U67995 | | AAB39620 | | Rattus norvegicus stearyl-CoA desaturase 2 mRNA, partial cds. |
| U76997 | | AAB19066 | | Rattus norvegicus insulin-regulated membrane aminopeptidase IRAP mRNA, complete cds. |
| U77583 | CKIaL | AAB19228 | | Rattus norvegicus casein kinase I alpha L (CKIaL) mRNA, complete cds. |
| U78090 | | AAC34249 | | Rattus norvegicus potassium channel regulator 1 mRNA, complete cds. |
| U78116 | AZF5 | AAB36788 | | Rattus norvegicus zinc finger protein 5 (AZF5) mRNA, partial cds. |
| U90215 | | AAB49989 | | Rattus norvegicus polysialyltransferase mRNA, partial cds. |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | Description |
|--|--|---|---|
| X05472 | ORF 3 | CAA29033 | Rat 2.4 kb repeat DNA, right terminal region. |
| X53261 | | CAA37350 | R.norvegicus mRNA for protein kinase A catalytic subunit. |
| X56747 | | CAA40069 | Rat mRNA for fetal intestinal lactase-phlorizin hydrolase precursor, partial. |
| X60370 | | CAC16162 | R.norvegicus mRNA for microtubule associated protein 1B. |
| X60790 | PYBP2 | CAA43203 | Rat PYBP2 mRNA for pyrimidine binding protein 2. |
| X64600 | tgna1 | CAA45884 | R.norvegicus mRNA for the trans Golgi network specific integral membrane protein TGN41. |
| X80029 | hem2 | CAA56333 | R.norvegicus Hem-2 mRNA. |
| X89963 | TSP-4 | CAA62002 | R.norvegicus mRNA TSP-4 protein. |
| Y13336 | DAD-1 | CAA73780 | Rattus norvegicus DAD-1 gene. |
| Y16774 | Dri 27/ZnT4 | CAA76372 | Rattus norvegicus mRNA for Dri 27/ZnT4 protein, complete CDS. |
| Z18877 | | CAA79317 | R.norvegicus mRNA for 2'5' oligoadenylate synthetase. |
| Z21935 | | CAA79929 | R.norvegicus protein kinase rMNK2. |
| NM_023986 | Temo | NP_076476 | Rattus norvegicus TEMO (Temo), mRNA. |
| RATTUS00016 | mwgrat10K#6143 | u10860 | u10860_1 guanosine 5'-monophosphate synthetase - homo sapiens expression: heart strains: sprague_dawley wistar_kyoto gbp |
| RATTUS00092 | mwgrat10K#6206 | bc014875 | bc014875_1 unknown protein for mgc:6920 - mus musculus expression: liver heart brain kidney strains: shrsp sprague_dawley wistar_kyoto gbp |
| RATTUS00129 | mwgrat10K#6238 | q9hcc0 | non-biotin containing subunit of 3-methylcrotonyl-coa carboxylase ec 6.4.1.4 expression: heart kidney strains: shrsp wistar_kyoto trembl |
| RATTUS00221 | mwgrat10K#6320 | bc003290 | bc003290_1 cyclin i - mus musculus expression: kidney brain heart strains: shrsp sprague_dawley wistar_kyoto gbp |
| RATTUS00223 | mwgrat10K#6321 | q9p110 | pro1038 expression: liver heart kidney strains: shrsp sprague_dawley wistar_kyoto trembl |
| RATTUS00276 | mwgrat10K#8728 | q9qz87 | oda-8s protein; kidney expression: brain heart strains: sprague_dawley wistar_kyoto trembl |
| RATTUS00284 | mwgrat10K#6373 | ak008492 | ak008492_1 riken full-length enriched library, clone:2010300021 - mus musculus; heart kidney shrsp trembl o75319 pirt ec 3.1.3.41 expression: brain strains: wistar_kyoto gbp |

Figure 23

| Nucleotide GenBank Accession Number or Manufacturer | Gene Name or Manufacturer | Probe Name | Protein Product GeneBank | | Description |
|---|------------------------------|----------------|-------------------------------------|-----------------------|--|
| | | | Accession Number or Manufacturer | Sequence Reference | |
| RATTUS00285 | mwgrat10K#6374 | mwgrat10K#6374 | ai411608 | ai411608 | af411608_1 n4wbp5a nedd4 ww domain-binding protein 5a - mus musculus expression: liver heart brain strains: shrsp sprague_dawley wistar_kyoto gbp |
| RATTUS00379 | mwgrat10K#6453 | mwgrat10K#6453 | q9gz0 | q9gz0 | hypothetical 27.1 kda protein cdna flj12619 fis, clone n12m4001682 expression: liver brain heart strains: sprague_dawley, wistar_kyoto trembl |
| RATTUS00410 | mwgrat10K#6481 | mwgrat10K#6481 | bc006847 | bc006847 | bc006847_1 niken cdna 061001317 gene - mus musculus expression: liver heart strains: shrsp sprague_dawley wistar_kyoto gbp |
| RATTUS00415 | mwgrat10K#6485 | mwgrat10K#6485 | q9wvd5 | q9wvd5 | ornithine transporter expression: liver heart kidney strains: shrsp sprague_dawley wistar_kyoto trembl |
| RATTUS00434 | mwgrat10K#6501 | mwgrat10K#6501 | q9h3n4 | q9h3n4 | cisplatin resistance related protein crf8p expression: brain heart strains: shrsp sprague_dawley wistar_kyoto trembl |
| RATTUS00437 | mwgrat10K#6503 | mwgrat10K#6503 | bc014808 | bc014808 | bc014808_1 proline rich protein expressed in brain - mus musculus expression: liver heart brain kidney strains: shrsp sprague_dawley wistar_kyoto gbp |
| RATTUS00451 | mwgrat10K#6516 | mwgrat10K#6516 | q9han2 | q9han2 | pumilio 2; heart wistar_kyoto trembl q9erc7 expression: liver brain strains: shrsp sprague_dawley trembl |
| RATTUS00521 | mwgrat10K#6575 | mwgrat10K#6575 | ak009646 | ak009646 | ak009646_1 niken full-length enriched library, clone:2310036d22 - mus musculus expression: liver heart brain strains: shrsp wistar_kyoto gbp |
| RATTUS00525 | mwgrat10K#6579 | mwgrat10K#6579 | af237619 | af237619 | af237619_1 dual specificity phosphatase ts-dsp2 - mus musculus expression: heart strains: shrsp wistar_kyoto gbp |
| RATTUS00526 | mwgrat10K#6580 | mwgrat10K#6580 | ak009743 | ak009743 | ak009743_1 niken full-length enriched library, clone:2310042b03 - mus musculus expression: heart brain strains: shrsp sprague_dawley wistar_kyoto gbp |
| RATTUS00530 | mwgrat10K#6584 | mwgrat10K#6584 | q9nzj7 | q9nzj7 | mitochondrial carrier homolog 1 isoform b expression: brain kidney strains: shrsp trembl |
| RATTUS00553 | mwgrat10K#6606 | mwgrat10K#6606 | q9h5j2 | q9h5j2 | cdna: flj23389 fis, clone hep17027 expression: heart brain strains: sprague_dawley wistar_kyoto trembl |
| RATTUS00575 | mwgrat10K#6624 | mwgrat10K#6624 | q9jk95 | q9jk95 | p53 apoptosis-associated target expression: liver kidney heart strains: shrsp sprague_dawley wistar_kyoto trembl |
| RATTUS00704 | mwgrat10K#6738 | mwgrat10K#6738 | bc010856 | bc010856 | bc010856_1 unknown protein for mgc:9160 - homo sapiens expression: brain strains: sprague_dawley wistar_kyoto gbp |

Figure 23 12

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | Description |
|--|--|---|---|
| RATTUS00794 | mwgrat10K#6816 | ak007469 | ak007469_1 riken full-length enriched library, clone:1810013b01 - mus musculus expression: liver brain kidney strains: shrsprague_dawley wistar_kyoto gbp |
| RATTUS00848 | mwgrat10K#6864 | x61585 | x61585_1 polynucleotide adenyltransferase - bos taurus expression: liver heart kidney strains: shrsprague_dawley wistar_kyoto gbp |
| RATTUS00867 | mwgrat10K#6879 | o95205 | zinc finger protein expression: brain strains: shrsprague_dawley trembl |
| RATTUS00868 | mwgrat10K#6880 | bc006778 | bc006778_1 unknown protein for image:3589084 - mus musculus expression: brain strains: shrsprague_dawley wistar_kyoto gbp |
| ATTUS00870 | mwgrat10K#6881 | q83380 | envelope protein expression: liver brain strains: shrsprague_dawley wistar_kyoto trembl |
| ATTUS00904 | mwgrat10K#6910 | q9p1s0 | hdkb03p fragment expression: brain strains: shrsprague_dawley wistar_kyoto trembl |
| ATTUS00937 | mwgrat10K#6941 | q9ulf5 | kiaa1265 protein fragment expression: brain strains: shrsprague_dawley wistar_kyoto trembl |
| ATTUS01071 | mwgrat10K#7054 | bc003862 | bc003862_1 transmembrane 9 superfamily member 2 - mus musculus expression: liver heart kidney brain strains: shrsprague_dawley wistar_kyoto gbp |
| ATTUS01093 | mwgrat10K#7071 | q9y6r2 | embryonic lung protein expression: liver brain heart strains: shrsprague_dawley wistar_kyoto trembl |
| ATTUS01148 | mwgrat10K#7121 | l10426 | l10426_1 er81 ets-related protein - mus musculus expression: brain strains: shrsprague_dawley wistar_kyoto gbp |
| ATTUS01170 | mwgrat10K#7138 | ak020910 | ak020910_1 riken full-length enriched library, clone:a93003030101 - mus musculus expression: brain strains: shrsprague_dawley wistar_kyoto gbp |
| RATTUS01205 | mwgrat10K#7167 | ak006207 | ak006207_1 riken full-length enriched library, clone:1700021i06 - mus musculus expression: liver heart brain strains: shrsprague_dawley wistar_kyoto gbp |
| RATTUS01221 | mwgrat10K#7181 | aj278133 | aj278133_1 erd2.2 putative kdel receptor - mus musculus expression: liver kidney brain strains: shrsprague_dawley wistar_kyoto gbp |
| RATTUS01273 | mwgrat10K#7225 | caa03190 | sequence 2 from patent wo96/10636 expression: liver brain strains: shrsprague_dawley wistar_kyoto trembl |
| RATTUS01287 | mwgrat10K#7238 | ak011418 | ak011418_1 riken full-length enriched library, clone:2610016f14 - mus musculus expression: brain strains: shrsprague_dawley wistar_kyoto gbp |
| RATTUS01294 | mwgrat10K#7245 | q9nvt7 | cdna flj10651 fis, clone n12p2005868 expression: brain strains: shrsprague_dawley wistar_kyoto trembl |

| Nucleotide GenBank Accession Number or Manufacturer | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | Description |
|---|--|---|--|
| RATTUS01392 | mwgrat10K#7330 | ak009373 | ak009373_1 riken full-length enriched library, clone:2310015017 - mus musculus expression: liver brain strains: sprague_dawley wistar_kyoto gbp |
| RATTUS01404 | mwgrat10K#7342 | m59288 | m59288_1 ferrochelatase - mus musculus expression: liver brain strains: shrsp wistar_kyoto gbp |
| RATTUS01416 | mwgrat10K#7352 | af212995 | af212995_1 cul4b cullin cul4b - homo sapiens expression: liver strains: wistar_kyoto gbp |
| RATTUS01422 | mwgrat10K#7358 | ak005698 | ak005698_1 riken full-length enriched library, clone:1700007d05 - mus musculus expression: liver heart strains: sprague_dawley wistar_kyoto gbp |
| RATTUS01478 | mwgrat10K#7409 | cab69424 | sequence 13 from patent wo9826065 fragment expression: liver brain strains: shrsp sprague_dawley wistar_kyoto trembl |
| RATTUS01526 | mwgrat10K#7452 | q9wuz9 | nucleoside diphosphatase er-udpase expression: liver kidney strains: wistar_kyoto trembl |
| RATTUS01538 | mwgrat10K#7464 | bc012401 | bc012401_1 unknown protein for mgc:11724 - mus musculus expression: liver brain strains: shrsp sprague_dawley wistar_kyoto gbp |
| RATTUS01590 | mwgrat10K#7512 | q9h9h1 | cdna fj12755 fis, clone n12rp2001295, weakly zinc/cadmium resistance protein expression: liver brain strains: sprague_dawley wistar_kyoto trembl |
| RATTUS01595 | mwgrat10K#7517 | bc003454 | bc003454_1 riken cdna 1110021n07 gene - mus musculus expression: kidney heart strains: sprague_dawley wistar_kyoto gbp |
| RATTUS01656 | mwgrat10K#7570 | q9jk31 | alfa-associated factor expression: heart kidney brain strains: shrsp sprague_dawley wistar_kyoto trembl |
| RATTUS01669 | mwgrat10K#7583 | bc006941 | bc006941_1 sphingosine kinase 2 - mus musculus expression: kidney strains: shrsp wistar_kyoto gbp |
| RATTUS01679 | mwgrat10K#7592 | ak008666 | ak008666_1 riken full-length enriched library, clone:2210008a03 - mus musculus expression: kidney strains: shrsp wistar_kyoto gbp |
| RATTUS01713 | mwgrat10K#7622 | q9nqq7 | ba394o2.1 cgl-15 protein expression: brain heart kidney strains: shrsp sprague_dawley wistar_kyoto trembl |
| RATTUS01762 | mwgrat10K#7667 | q9h5w6 | cdna: fj22937 fis, clone kat07960 expression: liver brain kidney strains: shrsp sprague_dawley wistar_kyoto trembl |
| RATTUS01834 | mwgrat10K#9859 | q9jmf6 | fragment expression: kidney brain strains: shrsp wistar_kyoto trembl |
| RATTUS01846 | mwgrat10K#7749 | ax118871 | ax118871_1 homo sapiens sequence 35 from patent wo0129221 unnamed protein product expression: kidney strains: shrsp wistar_kyoto gbp |

Figure 23

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | | Description |
|--|--|---|----------|---|
| | | | | |
| RATTUS01882 | mwgrat10K#7785 | bc003936 | bc003936 | bc003936_1 unknown protein for mgc:7327 - mus musculus expression: brain strains: shrsp sprague_dawley gbp |
| RATTUS02017 | mwgrat10K#7912 | q9qxm0 | q9qxm0 | alpha/beta hydrolase-2 fold protein expression: liver strains: shrsp sprague_dawley trembl |
| RATTUS02037 | mwgrat10K#7932 | bc011313 | bc011313 | bc011313_1 unknown protein for mgc:19443 - mus musculus expression: liver brain strains: shrsp sprague_dawley gbp |
| RATTUS02056 | mwgrat10K#7949 | q9hc79 | q9hc79 | serine kinase expression: liver brain strains: shrsp trembl |
| RATTUS02104 | mwgrat10K#7991 | aj277386 | aj277386 | aj277386_1 p14 late endosomal/lysosomal mp1 interacting protein - mus musculus expression: brain heart strains: shrsp sprague_dawley gbp |
| RATTUS02120 | mwgrat10K#8006 | af077188 | af077188 | af077188_1 cul4a cullin 4a - homo sapiens expression: liver brain kidney strains: shrsp sprague_dawley gbp |
| RATTUS02168 | mwgrat10K#8052 | ak011126 | ak011126 | ak011126_1 riken full-length enriched library, clone:2600001b17 - mus musculus expression: brain heart strains: shrsp sprague_dawley gbp |
| RATTUS02183 | mwgrat10K#8067 | o00495 | o00495 | 26s proteasome subunit 9 expression: heart brain strains: shrsp sprague_dawley trembl |
| RATTUS02235 | mwgrat10K#8116 | x53247 | x53247 | x53247_1 member of ras gene family en-7 protein - mus musculus expression: kidney brain strains: sprague_dawley wistar_kyoto gbp |
| RATTUS02251 | mwgrat10K#8130 | cac24865 | cac24865 | sequence 3 from patent wo0100831 expression: liver heart brain kidney strains: shrsp sprague_dawley wistar_kyoto trembl |
| RATTUS02282 | mwgrat10K#8152 | af104398 | af104398 | af104398_1 cornichon - homo sapiens expression: liver brain heart strains: shrsp sprague_dawley wistar_kyoto gbp |
| RATTUS02294 | mwgrat10K#8162 | ak014369 | ak014369 | ak014369_1 riken full-length enriched library, clone:3300002i08 - mus musculus expression: brain heart strains: sprague_dawley wistar_kyoto gbp |
| RATTUS02298 | mwgrat10K#8166 | ak015239 | ak015239 | ak015239_1 riken full-length enriched library, clone:4930429h24 - mus musculus expression: heart brain strains: shrsp sprague_dawley wistar_kyoto gbp |
| RATTUS02333 | mwgrat10K#8195 | q9ugg6 | q9ugg6 | 39k3 protein expression: heart brain strains: sprague_dawley wistar_kyoto trembl |
| RATTUS02339 | mwgrat10K#8200 | q9jkw0 | q9jkw0 | arl-6 interacting protein-1 expression: liver kidney brain strains: shrsp sprague_dawley wistar_kyoto trembl |
| RATTUS02445 | mwgrat10K#8294 | | | expression: liver brain strains: shrsp sprague_dawley wistar_kyoto mwg own new gene sequence |

| Nucleotide GenBank Accession Number or Manufacturer | Gene Name or Manufacturer | Protein Product GeneBank Accession Number or Manufacturer | Description |
|---|------------------------------|--|--|
| RATTUS02490 | mwgrat10K#8335 | q9h871 | expression: kidney brain strains: shrsp wistar_kyoto mwg own new gene sequence cdna fj113910 fls, clone y79aa1000131; trembl q9h6w5 cdna: fj121795 hep00531 expression: liver strains: shrsp trembl |
| RATTUS02564 | mwgrat10K#8395 | | |
| RATTUS02579 | mwgrat10K#8408 | q9hbm3 | dipeptidyl peptidase 8 fragment expression: liver strains: shrsp trembl |
| RATTUS02653 | mwgrat10K#8468 | bc003862 | bc003862, 1 transmembrane 9 superfamily member 2 - mus musculus expression: liver heart kidney brain strains: shrsp sprague_dawley wistar_kyoto gbp |
| RATTUS02662 | mwgrat10K#8476 | q14667 | kiaa0100 protein expression: liver kidney heart brain strains: shrsp sprague_dawley wistar_kyoto trembl |
| RATTUS02688 | mwgrat10K#8499 | q9hsl9 | hypothetical 22.2 kda protein fragment expression: brain strains: wistar_kyoto trembl |
| RATTUS02717 | mwgrat10K#8524 | af295358 | af295358_1 unknown - mus musculus expression: brain strains: wistar_kyoto gbp |
| RATTUS02731 | mwgrat10K#85250 | ak017729 | ak017729_1 riken full-length enriched library, clone:5730494n06 - mus musculus; wistar_kyoto trembl cac25005 sequence 49 from patent wo0100806 precursor expression: brain strains: shrsp gbp |
| RATTUS02792 | mwgrat10K#8583 | u59321 | u59321_1 p72 dead-box protein p72 - homo sapiens expression: heart strains: wistar_kyoto gbp |
| RATTUS02814 | mwgrat10K#8598 | u58135 | u58135_1 poly a polymerase v - mus musculus; heart trembl q9r1r3 testis-specific expression: liver kidney brain strains: shrsp wistar_kyoto gbp |
| RATTUS02918 | mwgrat10K#8683 | q92544 | myeloblast kiaa0255 expression: liver strains: wistar_kyoto trembl |
| RATTUS02943 | mwgrat10K#8699 | q9h2j3 | npd016 expression: liver strains: wistar_kyoto trembl |
| RATTUS02971 | mwgrat10K#8723 | bc002137 | bc002137_1 cg13018 gene product - mus musculus expression: liver strains: wistar_kyoto gbp |
| RATTUS03203 | mwgrat10K#8914 | q9y6a4 | transcription factor lib; trembl p70212 hypothetical 22.7 kda protein expression: liver brain strains: sprague_dawley wistar_kyoto trembl |
| RATTUS03223 | mwgrat10K#8928 | q9ji10 | lmbr1 long form expression: brain strains: sprague_dawley trembl |
| RATTUS03260 | mwgrat10K#9233 | q9y449 | traf4-associated factor 2 fragment; shrsp expression: brain strains: sprague_dawley trembl |
| RATTUS03288 | mwgrat10K#8981 | o15194 | ya22 protein hya22; kidney wistar_kyoto expression: brain strains: sprague_dawley trembl |
| RATTUS03326 | mwgrat10K#9012 | bc007154 | bc007154_1 unknown protein for image:3485091 - mus musculus expression: brain strains: sprague_dawley gbp |

Figure 23

| Nucleotide GenBank | | Protein Product | |
|--------------------|---------------------------|-----------------|--|
| Accession Number | Gene Name or Manufacturer | GeneBank | Accession Number |
| or Manufacturer | Probe Name | or Manufacturer | or Manufacturer |
| Sequence ID | Sequence ID | Sequence | Sequence |
| RATTUS03387 | mwgrat10K#9060 | ak003050 | ak003050 |
| | | | ak003050_1 riken full-length enriched library, clone:0710008m05 - mus musculus expression: heart strains: sprague_dawley gbp |
| RATTUS03472 | mwgrat10K#9126 | u62325 | u62325 |
| RATTUS03489 | mwgrat10K#9139 | q9nt50 | q9nt50 |
| RATTUS03495 | mwgrat10K#9144 | q9wuz9 | q9wuz9 |
| RATTUS03510 | mwgrat10K#9158 | o75071 | o75071 |
| RATTUS03523 | mwgrat10K#9169 | al356440 | al356440 |
| | | | al356440_1 dj299f11.1 dj299f11.1 d.melanogaster protein cg14464 - homo sapiens expression: liver strains: sprague_dawley gbp |
| IATTUS03577 | mwgrat10K#9213 | o35963 | o35963 |
| IATTUS03642 | mwgrat10K#9265 | cac09285 | cac09285 |
| IATTUS03669 | mwgrat10K#9288 | bc009494 | bc009494 |
| IATTUS03700 | mwgrat10K#9318 | q9nql3 | q9nql3 |
| IATTUS03772 | mwgrat10K#9332 | u95498 | u95498 |
| IATTUS03793 | mwgrat10K#9398 | o75061 | o75061 |
| IATTUS03819 | mwgrat10K#9421 | o75061 | o75061 |
| IATTUS03860 | mwgrat10K#9455 | q9y4c4 | q9y4c4 |
| IATTUS03883 | mwgrat10K#9483 | q9ijt5 | q9ijt5 |
| RATTUS03951 | mwgrat10K#9525 | o00495 | o00495 |
| RATTUS03971 | mwgrat10K#9537 | x61585 | x61585 |
| | | | x61585_1 polynucleotide adenyllyltransferase - bos taurus expression: liver heart kidney strains: shrsp wistar_kyoto gbp |
| RATTUS04030 | mwgrat10K#9583 | bc002867 | bc002867 |
| RATTUS04038 | mwgrat10K#9589 | bc013036 | bc013036 |
| RATTUS04052 | mwgrat10K#9603 | q9h4p0 | q9h4p0 |
| RATTUS04155 | mwgrat10K#9696 | | |
| | | | expression: heart strains: sprague_dawley mwg own new gene sequence |

Figure 23 17

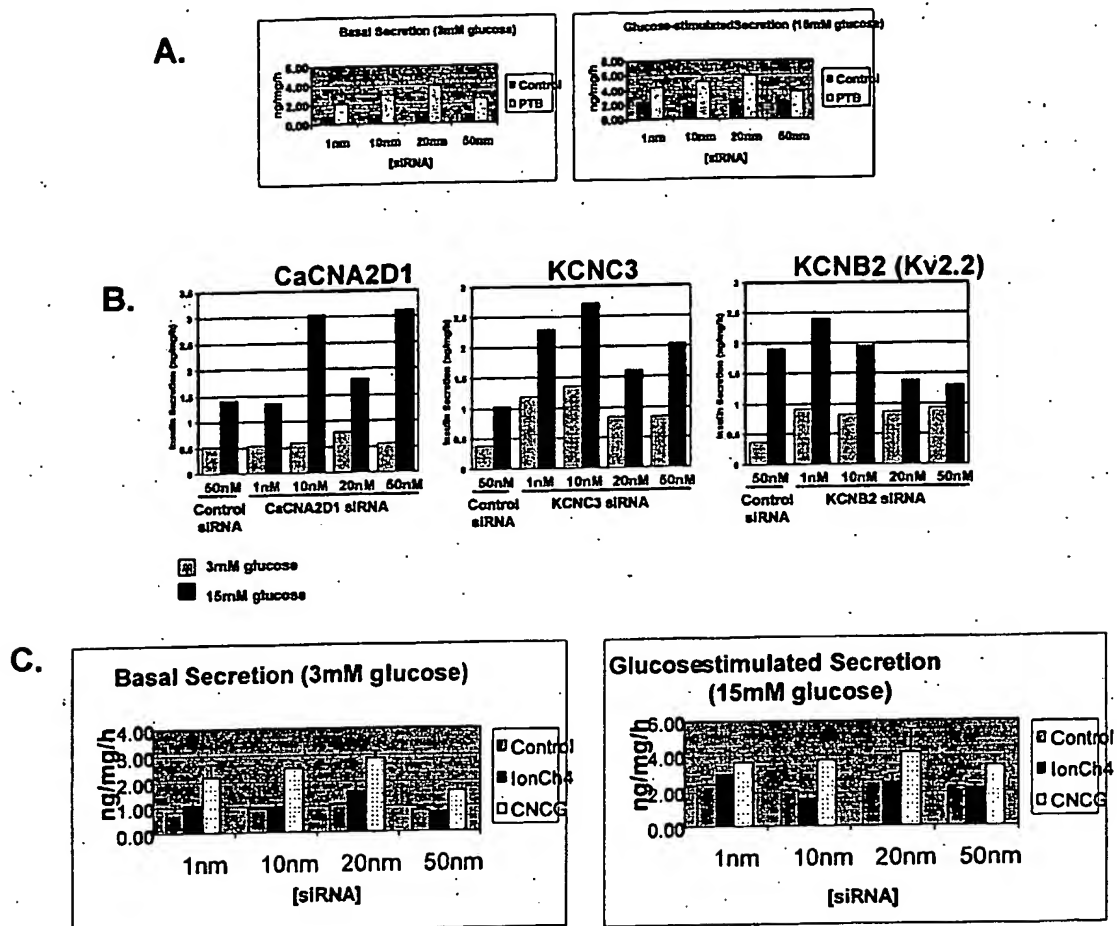


Figure 24

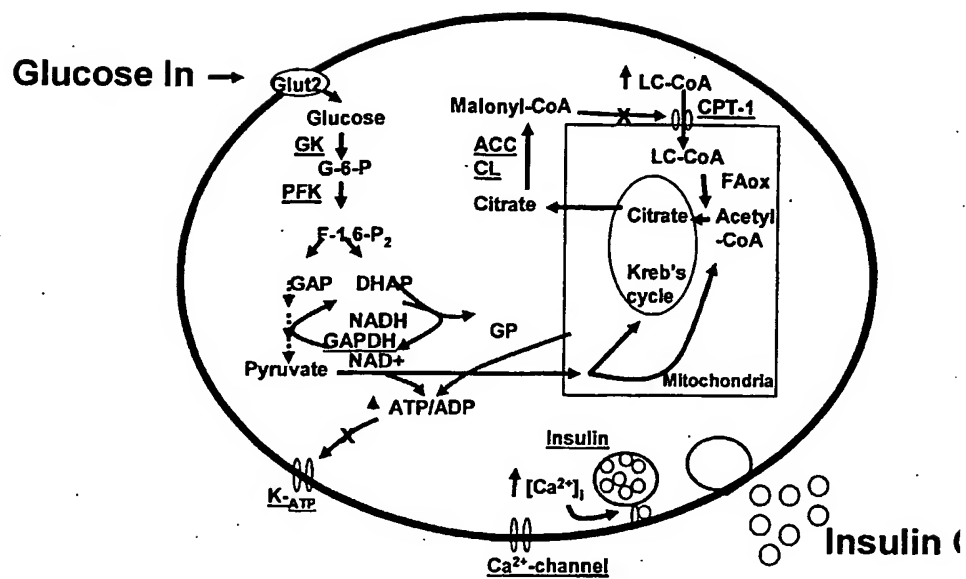


Figure 25

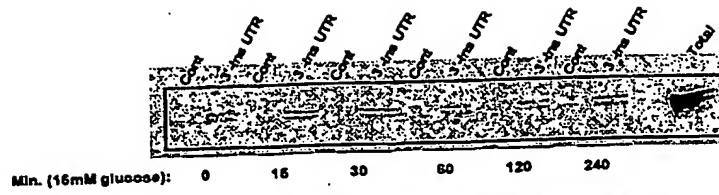


Fig. 26A

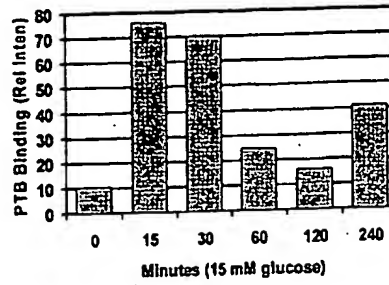


Fig. 26B

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | |
|--|--|---|--|
| | | Kinases | |
| NM_031081 | Pdpk1 | Rattus norvegicus 3-phosphoinositide dependent protein kinase-1 (Pdpk1), mRNA. | |
| NM_022799 | Nucks | Rattus norvegicus nuclear ubiquitous casein kinase 2 (Nucks), mRNA. | |
| NM_019248 | Ntrk3 | Rattus norvegicus neural receptor protein-tyrosine kinase (Ntrk3), mRNA. | |
| NM_053585 | Madd | Rattus norvegicus MAP-kinase activating death domain (Madd), mRNA. | |
| NM_022627 | Prkab2 | Rattus norvegicus AMP-activated protein kinase beta-2 regulatory subunit (Prkab2), mRNA. | |
| NM_012727 | Camk4 | Rattus norvegicus calcium/calmodulin-dependent protein kinase IV (Camk4), mRNA. | |
| NM_012713 | Prkcb1 | Rattus norvegicus protein kinase C, beta 1 (Prkcb1), mRNA. | |
| NM_013218 | Ak3 | Rattus norvegicus adenylate kinase 3 (Ak3), mRNA. | |
| NM_017246 | Map2k5 | Rattus norvegicus mitogen activated protein kinase 5 (Map2k5), mRNA. | |
| AB040531 | RH2K | Rattus norvegicus mRNA for RH2K2, complete cds. | |
| U39572 | | Rattus norvegicus phosphatidylinositol 4-kinase mRNA, complete cds. | |
| NM_012565 | Gck | Rattus norvegicus glucokinase (Gck), mRNA. | |
| NM_032080 | Gsk3b | Rattus norvegicus glycogen synthase kinase 3 beta (Gsk3b), mRNA. | |
| NM_080584 | Phkg2 | Rattus norvegicus phosphorylase kinase, gamma 2 (testis) (Phkg2), mRNA. | |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | |
|--|--|---|--|
| | | Phosphatases | |
| NM_012637 | Plpn1 | Rattus norvegicus protein tyrosine phosphatase, non-receptor type 1 (Plpn1), mRNA. | |
| NM_019253 | Plpn5 | Rattus norvegicus protein tyrosine phosphatase, non-receptor type 5 (Plpn5), mRNA. | |
| NM_010244 | Plpn5f | Rattus norvegicus protein tyrosine phosphatase, non-receptor type 5 (Plpn5f), mRNA. | |

Figure 27

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank Accession Number or Manufacturer Sequence Reference | Ion Channels/Regulators of Ion channels |
|--|--|---|--|
| | | | |
| NM_013080 | Piprz1 | NP_037212 | Rattus norvegicus protein tyrosine phosphatase, receptor-type, Z polypeptide 1 (Piprz1), mRNA. |
| NM_053883 | Dusp6 | NP_446335 | Rattus norvegicus dual specificity phosphatase 6 (Dusp6), mRNA. |
| NM_057115 | Pipn12 | NP_476456 | Rattus norvegicus protein tyrosine phosphatase, non-receptor type 12 (Pipn12), mRNA. |
| NM_013098 | G6pc | NP_037230 | Rattus norvegicus glucose-6-phosphatase, catalytic (G6pc), mRNA. |
| AB040531 | RH2K | BA96496 | Rattus norvegicus mRNA for RH2K2, complete cds. |
| AF013598 | | AAB69328 | Rattus norvegicus proton gated cation channel DRASIC mRNA, complete cds. |
| NM_031548 | Scnn1a | NP_113736 | Rattus norvegicus sodium channel, nonvoltage-gated, type 1, alpha polypeptide (Scnn1a), mRNA. |
| NM_012919 | Cacna2d1 | NP_037051 | Rattus norvegicus calcium channel, voltage-dependent, alpha2/delta subunit 1 (Cacna2d1), mRNA. |
| NM_013192 | Kcnj6 | NP_037324 | Rattus norvegicus potassium inwardly-rectifying channel, subfamily J, member 6 (Kcnj6), mRNA. |
| U78090 | | AAC34249 | Rattus norvegicus potassium channel regulator 1 mRNA, complete cds. |
| AF290212 | | AAG35186 | Rattus norvegicus calcium channel alpha-1-G subunit mRNA, complete cds. |
| NM_053497 | Cnng | NP_445949 | Rattus norvegicus cyclic nucleotide-gated cation channel (Cnng), mRNA. |
| Y14635 | | CAA74979 | Rattus norvegicus mRNA for proton-gated cation channels modulatory subunit |
| AJ003065 | | CAA05839 | Rattus norvegicus mRNA for Kir2.4, inwardly rectifying potassium channel. |
| NM_031828 | Kcma1 | NP_114016 | Rattus norvegicus potassium large conductance calcium-activated channel, subfamily M, alpha member 1 (Kcma1), mRNA. |
| NM_054000 | Kcnb2 | NP_446452 | Rattus norvegicus potassium voltage gated channel, Shab-related subfamily, member 2 (Kcnb2), mRNA. |
| NM_021853 | Slack | NP_068625 | Rattus norvegicus potassium channel subunit (Slack) (Slack), mRNA. |
| NM_019313 | Kcnn1 | NP_062186 | Rattus norvegicus potassium intermediate/small conductance calcium-activated channel, subfamily N, member 1 (Kcnn1), mRNA. |
| NM_013125 | Scn5a | NP_037257 | Rattus norvegicus sodium channel, voltage-gated, type V, alpha polypeptide (Scn5a), mRNA. |
| AJ309926 | asic 1b | CAC44267 | Rattus norvegicus mRNA for ion channel (asic 1b gene). |
| NM_053806 | Kcnk6 | NP_446258 | Rattus norvegicus potassium channel, subfamily K, member 6 (TWIK-2) (Kcnk6), mRNA. |

Figure 27

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank | | Transports |
|--|--|-------------------------------------|-----------------------|--|
| | | Accession Number or Manufacturer | Sequence Reference | |
| AB023645 | ccc6 | BAB40440 | | Rattus norvegicus ccc6 mRNA for cation-chloride cotransporter 6, complete cds. |
| AF239262 | oatpE | AAK30042 | | Rattus norvegicus organic anion transporter E (oatpE) mRNA, complete cds. |
| AF273024 | | AAF81796 | | Rattus norvegicus amino acid system A transporter mRNA, complete cds. |
| AB000280 | PHT1 | BAA20489 | | Rattus norvegicus mRNA for peptide/histidine transporter, complete cds. |
| NM_017348 | CHOT1 | NP_059044 | | Rattus norvegicus choline transporter (CHOT1), mRNA. |
| AF268030 | | AAF72546 | | Rattus norvegicus copper transporter 1 mRNA, complete cds. |
| NM_022866 | Sic13a3 | NP_074057 | | Rattus norvegicus solute carrier family 13 (sodium-dependent dicarboxylate transporter), member 3 (Sic13a3), mRNA. |
| AJ315643 | Hmit | CAC51117 | | Rattus norvegicus mRNA for proton myo-inositol symporter (Hmit gene). |
| U55816 | KCC2 | AAC52635 | | Rattus norvegicus furosemide-sensitive K-Cl cotransporter (KCC2) mRNA, complete cds. |
| NM_013034 | Sic6a4 | NP_037166 | | Rattus norvegicus solute carrier family 6, member 4 (Sic6a4), mRNA. |
| NM_012879 | Sic2a2 | NP_037011 | | Rattus norvegicus solute carrier family 2, member 2 (Sic2a2), mRNA. |

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product GeneBank | | Proteases/Peptidases |
|--|--|-------------------------------------|-----------------------|---|
| | | Accession Number or Manufacturer | Sequence Reference | |
| NM_012836 | Cpd | NP_036968 | | Rattus norvegicus carboxypeptidase D (Cpd), mRNA. |
| AF202454 | | AAF17575 | | Rattus norvegicus testis ubiquitin specific processing protease mRNA, complete cds. |
| NM_017145 | Mcpt1 | NP_058841 | | Rattus norvegicus mast cell protease 1 (Mcpt1), mRNA. |

Figure 27

86/89

| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | |
|--|--|--|--|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | Receptors |
| NM_019246 | Pcsk7 | NP_062119 | Rattus norvegicus proprotein convertase subtilisin / kexin, type 7 (Pcsk7), mRNA. |
| NM_017138 | Lamr1 | NP_058834 | Rattus norvegicus laminin receptor 1 (67kD, ribosomal protein SA) (Lamr1), mRNA. |
| NM_012637 | Ptpn1 | NP_036769 | Rattus norvegicus protein tyrosine phosphatase, non-receptor type 1 (Ptpn1), mRNA. |
| NM_016996 | Casr | NP_058692 | Rattus norvegicus calcium-sensing receptor (Casr), mRNA. |
| NM_019248 | Ntrk3 | NP_062121 | Rattus norvegicus neural receptor protein-tyrosine kinase (Ntrk3), mRNA. |
| U47331 | | AAA88788 | Rattus norvegicus metabotropic glutamate receptor 4b mRNA, complete cds. |
| NM_019328 | Nr4a2 | NP_062201 | Rattus norvegicus nuclear receptor subfamily 4, group A, member 2 (Nr4a2), mRNA. |
| NM_012869 | Npy5r | NP_037001 | Rattus norvegicus neuropeptide Y receptor Y5 (Npy5r), mRNA. |
| NM_019253 | Ptpn5 | NP_062126 | Rattus norvegicus protein tyrosine phosphatase, non-receptor type 5 (Ptpn5), mRNA. |
| NM_052807 | Igf1r | NP_434694 | Rattus norvegicus insulin-like growth factor 1 receptor (Igf1r), mRNA. |
| NM_013080 | Ptpnz1 | NP_037212 | Rattus norvegicus protein tyrosine phosphatase, receptor-type, Z polypeptide 1 (Ptpnz1), mRNA. |
| NM_031628 | Nr4a3 | NP_113816 | Rattus norvegicus nuclear receptor subfamily 4, group A, member 3 (Nr4a3), transcript variant 1, mRNA. |
| NM_017011 | Gnm1 | NP_058707 | Rattus norvegicus glutamate receptor, metabotropic 1 (Gnm1), mRNA. |
| NM_013091 | Tnfrsf1a | NP_037223 | Rattus norvegicus tumor necrosis factor receptor superfamily, member 1a (Tnfrsf1a), mRNA. |
| NM_017071 | Insr | NP_058767 | Rattus norvegicus insulin receptor (Insr), mRNA. |
| AF161588 | Gabarap | AAD47643 | Rattus norvegicus GABA-A receptor-associated protein (Gabarap) mRNA, complete cds. |
| NM_057115 | Ptpn12 | NP_476456 | Rattus norvegicus protein tyrosine phosphatase, non-receptor type 12 (Ptpn12), mRNA. |
| NM_012528 | Chmb1 | NP_036660 | Rattus norvegicus cholinergic receptor, nicotinic, beta polypeptide 1 (Chmb1), mRNA. |
| AF010293 | U131 | AAB66333 | Rattus norvegicus olfactory receptor (U131) mRNA, complete cds. |
| NM_012957 | Gabbr2 | NP_037089 | Rattus norvegicus gamma-aminobutyric acid receptor, subunit beta 2 (Gabbr2), mRNA. |
| NM_012959 | Gfra1 | NP_037091 | Rattus norvegicus glial cell line derived neurotrophic factor family receptor alpha 1 (Gfra1), mRNA. |
| NM_053296 | Girb | NP_445748 | Rattus norvegicus glycine receptor, beta subunit (Girb), mRNA. |
| AF205193 | | AAF19028 | Rattus norvegicus glutamate receptor interacting protein 2 mRNA, complete cds. |
| Z23272 | | CAA80810 | R. norvegicus PACAP receptor, hip-hop1 splice variant, complete CDS. |
| AF230645 | | AAF36975 | Rattus norvegicus testis-type galactosyl receptor mRNA, complete cds. |

Figure 27

| | | | |
|-----------|----------|-----------|--|
| NM_012896 | Adora3 | NP_037028 | Rattus norvegicus adenosine A3 receptor (Adora3), mRNA. |
| NM_024146 | Fgfr1 | NP_077060 | Rattus norvegicus Fibroblast growth factor receptor 1 (Fgfr1), mRNA. |
| NM_022186 | Nrbf2 | NP_071522 | Rattus norvegicus nuclear receptor binding factor 2 (Nrbf2), mRNA. |
| U22830 | | AAA91303 | Rattus norvegicus P2Y purinoceptor mRNA, complete cds. |
| NM_021745 | Nr1h4 | NP_068513 | Rattus norvegicus nuclear receptor subfamily 1, group H, member 4 (Nr1h4), mRNA. |
| NM_013124 | Pparg | NP_037256 | Rattus norvegicus peroxisome proliferator activated receptor, gamma (Pparg), mRNA. |
| AJ011370 | 5-HT4 | CAA09599 | Rattus norvegicus mRNA for serotonin 4 receptor, splice variant r5-HT4(e). |
| AF016387 | RXRgamma | AAD01591 | Rattus norvegicus retinoid X receptor gamma (RXRgamma) mRNA, partial cds. |
| NM_022212 | Insr | NP_071548 | Rattus norvegicus insulin receptor-related receptor (Insr), mRNA. |

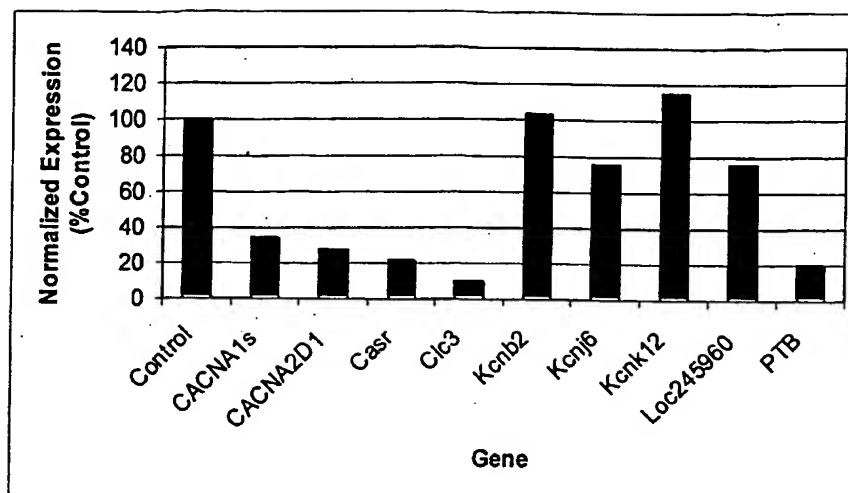
| Nucleotide GenBank Accession Number or Manufacturer Sequence ID | Gene Name or Manufacturer Probe Name | Protein Product | |
|--|--|--|--|
| | | GeneBank Accession Number or Manufacturer Sequence Reference | Transferases |
| NM_022635 | Cml4 | NP_072157 | Rattus norvegicus putative N-acetyltransferase Camello 4 (Cml4), mRNA. |
| NM_022280 | Lrat | NP_071616 | Rattus norvegicus lecithin-retinol acyltransferase (Lrat), mRNA. |
| X14211 | | CAA32428 | Rat mRNA for phenylethanolamine-N-methyltransferase (PNMT). |
| NM_031635 | Fut2 | NP_113823 | Rattus norvegicus fucosyltransferase 2 (Fut2), mRNA. |
| NM_013029 | Sial8c | NP_037161 | Rattus norvegicus sialyltransferase 8 C (Sial8c), mRNA. |
| NM_031980 | Ugt2b12 | NP_114186 | Rattus norvegicus UDP-glucuronosyltransferase (Ugt2b12), mRNA. |
| NM_022219 | Fut4 | NP_071555 | Rattus norvegicus alpha 1,3-fucosyltransferase Fuc-T (similar to mouse Fut4) (Fut4), mRNA. |
| NM_053437 | Dgat1 | NP_445889 | Rattus norvegicus diacylglycerol O-acyltransferase 1 (Dgat1), mRNA. |

Figure 27

| Nucleotide GenBank Accession Number or Manufacturer | Gene Name or Manufacturer | Protein Product | |
|---|------------------------------|-----------------|--|
| | | GeneBank | Accession Number |
| | | Sequence | Reference |
| NM_012747 | Stat3 | NP_036879 | Rattus norvegicus signal transducer and activator of transcription 3 (Stat3), mRNA |
| NM_017339 | Isl1 | NP_059035 | Rattus norvegicus ISL1 transcription factor, LIM/homeodomain 1 (Isl1), mRNA |
| NM_021770 | Olig1 | NP_068538 | Rattus norvegicus oligodendrocyte transcription factor 1 (Olig1), mRNA |

Figure 27

A.



B.

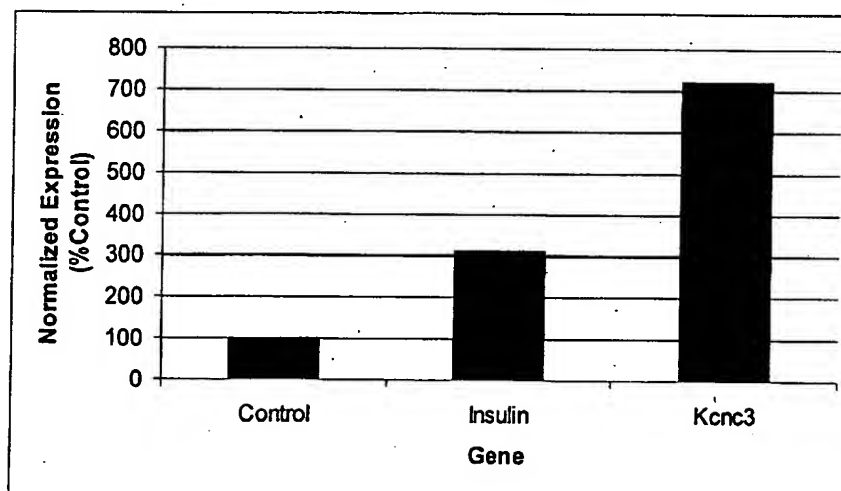


Figure 28

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pean (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR,
GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK,
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ning of each regular issue of the PCT Gazette.

(54) Title: METHODS FOR IDENTIFYING THERAPEUTIC TARGETS INVOLVED IN GLUCOSE AND LIPID METABO-
LISM

(57) Abstract: The identification and evaluation of mRNA and protein targets associated with RNA binding proteins or mRNP com-
plexes is described. In particular, the invention provides methods for identifying RNA binding proteins associated with physiological
pathways that participate in glucose and lipid metabolism and mRNAs that exhibit coordinated gene regulation across thoseMpath-
ways. Candidate targets are provided that are useful for the diagnosis or treatment of diseases related to diseases, such as disease
related to aberrant glucose and lipid metabolism, such as, for example, obesity, diabetes, and hypoglycemia.

WO 2004/092740 A3

INTERNATIONAL SEARCH REPORT

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 IPC 7 G01N33/68 G01N33/53

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC 7 G01N C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|--------------------------------------|
| X | PHELPS W. B.: "Innovative Systems Biology" 'Online! 6 November 2002 (2002-11-06), XP002291620 Retrieved from the Internet: URL: http://www.ribonomics.com/news/presentations/ribonomics_RNA_in_Drug_Development.pdf > 'retrieved on 2004-08-05! the whole document | 1-11, 14, 15, 18-20, 30, 37 |
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- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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& document member of the same patent family

Date of the actual completion of the international search

27 October 2004

Date of mailing of the international search report

04.01.05

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/010686

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| A | <p>KEENE JACK D ET AL: "Eukaryotic mRNPs may represent posttranscriptional operons" MOLECULAR CELL, vol. 9, no. 6, June 2002 (2002-06), pages 1161-1167, XP002291625 ISSN: 1097-2765</p> | |
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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/010686

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-20,25-30,37

screening methods involving the comparison of RNA or protein levels of at least one component of an isolated mRNP from two different cellular phenotypes or states (e.g. treated vs. untreated)

2. claims: 21-24

method for identifying a gene or gene product involved in a physiological pathway by isolating additional components of an mRNP complex that contains a component already known to be involved in said pathway

3. claims: 31,32

method for identifying an insulin production regulating protein agent characterized by its ability to bind to the 3' or 5' untranslated region of a preproinsulin mRNA

4. claim: 33

mRNP complex involved in glucose or lipid metabolism which comprises PTB protein and an mRNA associated with PTB

5. claims: 34-36

method for identifying a component of an mRNP complex by expression profiling of RNA with or without prior inhibition of expression of an RNA binding protein

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US2004/010686

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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